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President of the Congress

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Secretary General

BENT HARVALD
Vice-Secretary General

PART II

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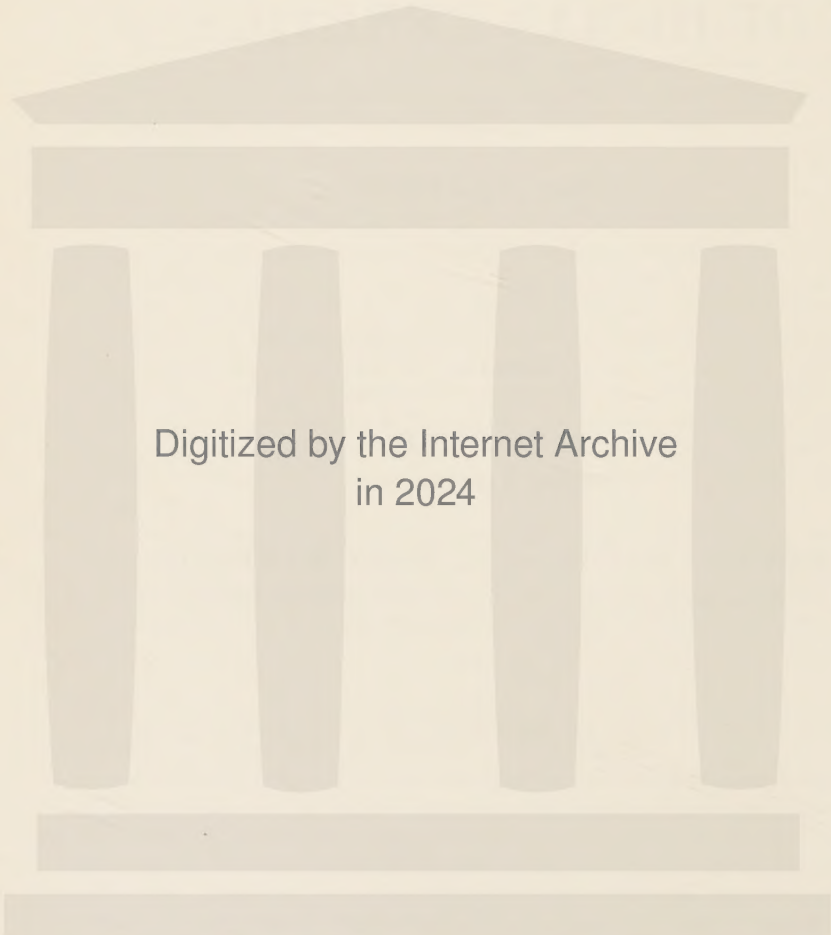

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PART II

Selection and the Structure of Human Populations

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Physical Anthropology

SELECTION AND THE STRUCTURE OF HUMAN POPULATIONS

Haldane, J. B. S.: Acta genet. *6*, 321–332, 1956/57

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NATURAL SELECTION IN MAN

By J. B. S. HALDANE

The consideration of natural selection is seriously handicapped by our vocabulary. To begin with, we use the same word for phenotypic and genotypic selection, though only the latter has any effect on future generations. If, in a pure line, one selects the heaviest beans, the beans of the next generation are no heavier than if one selects the lightest, as *Johannsen* first showed. Such selection will only have genetical results if a mutation occurs within a line. Except in the case of a very few characters whose genetical determination is simple and well understood, we can only measure phenotypic selection in man. We seldom know what fraction of the variance in the character considered is genetically determined, and sometimes we do not even know the organism whose genotype is relevant.

For example *Karn* and *Penrose* [1951] found that unusually light and heavy babies died more frequently at birth or in their first month than those of normal weight. This is pure phenotypic selection. By studying the children of sibs, *Robson* [1955] found correlation between the birth weight of children of sisters, but not between those of brothers or of brother and sister. No doubt the genotype of a baby has some influence on its birth weight, but this was too small for *Robson* to detect. The mother's genotype had a detectable influence. But *Robson*'s sample was not large enough to enable her to discover whether there was any selection of maternal genotypes by intranatal and neonatal mortality. I have little doubt that there is some such selection, but we do not know its intensity.

Secondly some measures of phenotypic selection are given in terms of the mean value of a character in selected individuals. *Lush* [1951] uses the term "selective differential" for the difference between the mean value of a character in the parents of the next generation (the parent of n children being counted n times) and the mean in the population from

which they are drawn. This can be compared with the "selective advance", which is the difference between such means in successive generations. This is a major contribution to the theory of artificial selection. But since natural selection usually weeds out extremes, it may be rather misleading when one is dealing with natural selection.

Haldane [1954] gave a wholly different measure. He compared the fraction of the whole population which survived over a certain period with the fraction of the group possessing the optimal phenotypic value which did so. For example *Karn* and *Penrose*'s data show that the death-rate in all the babies in their sample was about 4½%, that in the group whose weights lay between 7½ and 8½ pounds being about 1½%. Thus two thirds of all these deaths were phenotypically selective, and the total intensity of selection was 3%. Unfortunately we do not know what fraction of this 3% was also genotypic selection. But it is remarkable that by considering a single character, weight, no less than two thirds of all deaths in a critical period of life have been shown to be selective for it. No doubt most of the remaining 1½% of deaths are selective for characters not highly correlated with weight (e.g. anencephaly, spina bifida, heterozygosis for the D and d antigens). It may be that an equally large fraction of deaths at some other periods of life are phenotypically selective, if we knew what characters to measure or observe.

Another possible measure is the ratio of the variance of the survivors (or parents) to that of the whole population from which they are drawn. In fact this variance is reduced in all cases so far investigated. *Haldane* [1954] showed that if the distributions of the total population and the survivors are both normal, there is a simple relation between the second and third measures.

The measurement of phenotypic natural selection in man is extremely difficult for the following reason. A good deal of mortality occurs before birth. Even if its amount were accurately known, we should not know whether (to take one possible selection pressure) the mortality was greater in slowly growing than in rapidly growing embryos. Such a selection might have very important evolutionary effects.

Further, most studies giving data on natural selection in man only cover a fraction of the live cycle. Thus *Karn* and *Penrose* found optimal survival among babies of a particular weight during birth and the first month of life. If they could have followed them up it is very possible that the optimum survival up to, say, 20 years would have been in a different group, the maximum fertility in still another group, and so on. And these groups would have been based on weight at birth. Since birth weight and

adult weight are not very highly correlated, we cannot argue from the higher mortality of overweight adults to a higher mortality in adult life of individuals who are overweight as babies.

Important data have been accumulated on the fertility of adults in relation to their economic position, their intelligence, and so on. However they had only been classified as adults, that is to say after they had been exposed to prenatal and juvenile selection. In view of the high mortality of idiots and imbeciles, it is at least probable that pre-adult selection goes some way towards counteracting the genetical effects of the lesser fertility of more intelligent parents.

In spite of this, data on natural selection in man are more adequate than those concerning any animal species in its natural habitat. In particular it is quite impossible in most animal species to estimate the number of offspring begotten by a given male under natural conditions, though it is possible to do so in monogamous species such as most birds. So data on natural selection in man are not only of interest to anthropologists, physicians, sociologists, and so on, but to every student of evolution.

Genotypic selection is, theoretically, easier to measure. To determine whether the frequency of a given allel will alter, and if so how much, we merely require to know the mean numbers of offspring produced by parents homozygous for it, heterozygous for it, and without it. Unfortunately we only know this for selectively nearly neutral genes such as the M and N blood type genes, and for genes causing a grossly pathological condition such as haemophilia or microcythaemia.

Evolution is normally an extremely slow process. *Haldane* [1949a] (see also *Simpson* [1953]) showed that in several lines such as horses and dinosaurs the mean length of skeletal dimensions had seldom changed by much over 5% per million years over long periods, though rapid phases of evolution separated by longer quiet periods were not excluded. Human skull height had probably evolved much more rapidly than this during the last million years or so. But natural selection can be far more intense than *Darwin* believed. *Dobzhansky* and his colleagues, in particular, have shown that natural selection in several species of Drosophila is very intense, some common genotypes having a fitness less than half that of others. But this intense natural selection does not produce rapid evolution. On the contrary, it stabilizes the species.

In fact natural selection may be compared with the forces of physics, and particularly with gravitation. Gravitation can certainly produce short-time dynamical effects, such as the fall of unsupported bodies, and long-term effects such as the erosion of mountain ranges and probably the

condensation of gas clouds into stars. But it is usually balanced either by rigidity (electrostatic repulsion of atomic shells) which prevents houses from falling down, or by "centrifugal force", which prevents the moon from falling down. Similarly natural selection can produce evolutionary change, but is generally prevented from doing so by other dynamical processes. The most important of these are mutation, segregation, and migration.

Mutation prevents natural selection from extinguishing genes such as that for haemophilia. There is an approximate equilibrium with a frequency of about 5×10^{-5} haemophilics among males at birth. The fitness of haemophilics is less than half. So a gene with a similar mutation rate reducing the fitness by only 1% would have a frequency of the order of 0.5%. I have no doubt that such genes exist and are important, and that some of them are socially valuable.

Segregation preserves two or more allels at one locus in all cases where the heterozygote is fitter than either homozygote. The most striking case yet known in man is the polymorphism for haemoglobin studied by *Allison* [1954a, 1956], but this effect may well be the main cause of human genetical polymorphism.

In the absence of migration the human beings in any area would probably become homozygous for a great many genes, including the principal genes for skin colour. The skin pigmentation would probably be minimal in subarctic regions, with maxima in some tropical regions, and a smaller maximum in the arctic, where skin pigment may give protection against light reflected from snow. Migration preserves a degree of polymorphism in most regions. In parenthesis it may be remarked that there is no reason to suppose that races which are adapted to the natural climates of their native lands are adapted to the novel climates produced by artificial heating, artificial lighting, and more recently, artificial cooling, of human dwellings.

Mather [1953] and *Waddington* [1953] tried to classify natural selection by its effects (see also *Simpson* [1953]). *Mather* wrote of directional selection, which changes the mean value of a character, stabilizing selection (cf. *Schmalhausen* [1949]), which reduced its variance, and disruptive selection, which increases the variance, and may lead to a bimodal distribution. Disruptive selection certainly occurs when a species forms local races, but I think it very rarely occurs within a gamodeme, or population mating together. *Waddington* dichotomised *Schmalhausen*'s stabilizing selection into stabilizing selection proper, that is to say the elimination of genotypes which develop into any of a wide range of

phenotypes, and normalizing selection, that is to say the elimination of genotypes which usually develop into a phenotype whose mean differs greatly from the normal. They cannot of course be distinguished when only phenotypic selection is observed. Further selection which is directional on phenotypes may be non-directional on genotypes, and conversely. We shall, I believe, need a separate vocabulary for the different types of phenotypic and genotypic selection. To take a well-known human example, selection at the human Rh locus due to neonatal jaundice caused by the D antigen is phenotypically disruptive but genotypically directional. A fraction of *Dd* zygotes is eliminated. The survivors are more antigenically variable than the population from which they are drawn. But the genetical effect of this is to eliminate the *d* gene or more rarely the *D* gene, and not to produce populations dimorphic for *DD* and *dd*.

Dr. *Spurway* suggests that a beginning might be made by using one of a pair of synonymous words or phrases for phenotypic, the other for genotypic selection. Thus the older word fitness might refer exclusively to phenotypic fitness, the newer phrase, adaptive value, to genotypic fitness. Centripetal selection might be used for selection reducing the phenotypic variance, stabilizing and normalizing selection for the effects on genotype frequencies.

After these prolegomena I pass to the consideration of particular examples of natural selection in man. The easiest case to consider is the equilibrium between selection and the mutation of "dominants" or sex-linked recessive genes. By a "dominant" I mean a gene which causes abnormality when heterozygous. The homozygotes are usually unknown. When known they are lethal or sublethal. *Penrose* and *Haldane* [1935] first analysed such cases. *Kemp* and his colleagues have carried out the analysis on a much larger scale, and greatly increased our knowledge. Natural selection against some of these genes is very intense. It is falling off in intensity through medical care. But it is most desirable that this fall should be counteracted by artificial selection. Haemophilics, for example, should be told that it is their duty to refrain from parenthood, and their wives or prospective wives should realise that the daughters of haemophilics have the lamentable choice between sterility and watching their sons die.

The measurement of the fitness of human abnormals is very difficult. In the first place it is essential that only probands should be used. If all members of a pedigree are used, then the members studied in earlier generations will include a large fraction of those rare abnormals who, in spite of their disability, had large families. The apparent fitness will be far

too high. On the other hand the probands are usually those who have survived for some years. Statistics of infantile deaths from haemophilia are, for example, very suspect. Various haemorrhagic diseases, including vitamin K deficiency, may be described as haemophilia in death certificates. Alternatively a physician may be loth to describe a death as haemophilia if no previous case is known in the family.

Precision will only be reached in a country such as Sweden or Denmark, with a good medical service, a not too mobile population, and institutes which do not depend on a single director. A full study will require the following up of a hundred or so abnormals at least up to the age when almost all their children have been born. This will require the devoted work of observers who accumulate data in the hope that their successors will draw conclusions from them. Unless such a survey is planned with exceptional care it will probably be a failure.

Where a dominant, such as renal glycosuria, is quite rare, but apparently harmless, there is a real problem. Does such a gene arise very rarely by mutation, or does it after all reduce the life span or fertility appreciably? With the socialization of medicine we may look forward to a time when, in the more progressive nations, everyone will at some time be tested for glycosuria, and it will be possible to answer these questions. Other dominants such as the gene causing absence or reduction of lateral incisors may have no selective disadvantage when heterozygous, though *Mandeville*'s [1950] work suggests that homozygotes may be handicapped. Since the human teeth appear to suffer from overcrowding it will ultimately be important to know whether or not such genes may be expected to spread, and if so whether this spread should be encouraged.

Autosomal recessives are commonly lethal or sublethal. *Bell* [1941] showed that the recessive forms of several diseases manifest themselves earlier, and are therefore subject to stronger natural selection, than the dominant forms. In some cases (e.g. the amaurotic idiocies) the data are consistent with the hypothesis that these genes have no selective effect in heterozygotes, and that mutation is balanced by the elimination of homozygotes. But it is quite impossible to prove that the fitness of heterozygotes is so near normal that this assumption is justified. Thus supposing that the frequency of a lethal recessive condition is about 1 in 40,000 births, the frequency of the recessive gene will be somewhat below 0.5%, as some of the recessives will be derived from consanguineous unions. If the fitness of heterozygotes were 0.5% greater than the average, this would be more than sufficient to keep the gene in being without any mutation. If it were 1% below the average, the mutation rate would

have to be about three times that required if it were normal. Such differences could only be detected by the study of about 100,000 heterozygotes.

However a possibility exists, which is illustrated by the work of *Cain* and *Sheppard* [1952] and *Sheppard* [1954] on *Cepea nemoralis*. They had reason to suppose that certain colour types were eliminated in certain environments, for example yellows in dark beech woods. By studying the shells of those killed by thrushes (*Turdus ericetorum*) they found that on a dark background, thrushes killed many more yellow than brown snails, even though the total fraction killed by thrushes per season was only about 3%. It might then be found that, for example, heterozygotes for the amaurotic idiocies were particularly liable to certain nervous diseases or psychoses, or that heterozygotes for *Wilson*'s disease were particularly liable to liver disease. It would be much harder to prove that heterozygotes enjoyed some particular advantage.

In the case of common lethal and sublethal recessives, only a fantastically high mutation rate could keep the gene in being, and we have to look for evidence that the recessive is favoured by natural selection. The first case of this kind was proved by *Beet* [1948] and *Allison* [1954b, 1956] for sickle-cell anaemia. The heterozygotes are resistant to *Plasmodium falciparum*. It is very likely that heterozygotes for microcythemia (thalassemia, *Cooley*'s anaemia) are resistant to some form of malaria, but malaria has been so effectively reduced round the Mediterranean that it will be hard to prove this. The commonest known lethal recessive in Western Europe and North America is cystic fibrosis of the pancreas. Here according to *Goodman* and *Reed* [1952], the frequency of recessives is 7 to 10×10^{-4}, so the gene frequency is about .03. *di St. Agnese*, *Darling*, *Perera* and *Shea* [1953] find that the salt content of the sweat of heterozygotes is, on an average, somewhat supernormal. It is hard to see what advantage this could confer. But, for equilibrium, a selective advantage of about 3% would be needed. It may be too late to look for such an advantage. Professor *Penrose* has suggested in conversation that heterozygosity may have conferred protection against some now extinct disease.

The blood group genes show indications of a very complex situation. On the one hand there may be foetal elimination of heterozygotes in some recessive mothers. On the other hand there are differences in morbidity from certain stomach diseases. It seems clear that the biochemical nature of mucus in various secretions depends on genes at the ABO locus, the *Lewis* locus, and the secretor locus, and presumably all are concerned

in the aetiology of these diseases. There may well also be some interaction with the gene for fibrocystic pancreatitis. One naturally looks for a system of selective "forces" which might lead to some kind of equilibrium. I think it unlikely that this will be discovered until it is possible, without genetical data, to decide whether, for example, a person of phenotype A_1 is in fact $A_1 A_1$, $A_1 A_2$ or $A_1 0$.

It is my considered opinion that these questions will not be cleared up until we know a good deal more concerning the physiology and biochemistry of gene action.

This is even more so when we come to consider selection for quantitative characters such as birth weight and intellectual capacity. In each of these cases there is a zone of optimal fitness. It is difficult, as *Wright* [1935] first showed, to see how selection for a metrical character as such would preserve heterozygosis at more than one locus. In both of these cases many loci must be concerned. It therefore seems likely that heterozygosis, as such, at several loci makes for increased fitness. It seems to me more hopeful to look for discrete biochemical polymorphisms with clear genetical determination, and to hope that one of these will be correlated with a metrical character. I would urge that whenever a common immunological or biochemical polymorphism is found, at least rough biometrical work should be done on the different genotypes. Such work will inevitably be tedious and unrewarding. It is quite unlikely that the three genotypes defined by the *Smithies'* [1955] plasma proteins differ significantly in height, intelligence, hair colour, or any other simple metrical character. Nevertheless if they were found to do so a fundamental step forward in human genetics would have been made. The moment that even one pair of allels, both fairly common, and responsible for a component in a metrical character, have been discovered, it should be possible to discover something about the selective "forces" which are responsible for the genetical variance of that character. For it is abundantly clear that in the case of many metrical characters there is natural selection against extremes. We do not know exactly why this is so, except for such exceptional cases as achondroplastic dwarfism, where the lack of fitness is partly due to the fact that females are infertile on mechanical grounds.

Some years ago (*Haldane* [1949b]) I stated my belief that during the last 5000 years the main agents of natural selection in man had been infectious diseases. As soon as the inventions of agriculture and cities had made relatively dense human populations possible, such selective agencies as vertebrate predation ceased to be important, and diseases

facilitated by overcrowding took their place. From an evolutionary point of view this was, I believe, a misfortune. A man who can climb a tree when pursued by a lion is a better man in other respects than one who cannot. A man who can resist tuberculosis is, so far as we know, no better in other respects. He is probably worse. Infectious diseases have doubtless spread a great many previously rare genes through human populations. The fact that they were rare means that they mostly lowered the fitness of our ancestors. They probably lower our own, except in environments where the organism against which they confer resistance is fairly common. This is certainly true of the gene for sickle cell anaemia.

If, as has been claimed, with singularly little evidence, savages living in non-malarial regions are congenitally superior to men whose ancestors have been civilized for many generations, this should provisionally be ascribed to the fact that these ancestors have been selected for resistance to infectious diseases, rather than to the fact that they have been protected from tigers, frost, and the like.

The abolition of infectious diseases, which is now a possibility, and may be a reality in fifty years, should lead not only to an immediate improvement in human physique, but to a progressive improvement through many centuries.

It is nevertheless true that natural selection in man has been less stringent than in some other animal species, as a result of the human tendency not merely to protect children but weak members of the species. So long as natural selection was regarded as primarily directive, this appeared to be a check on evolutionary progress. We now see that selection is mainly a stabilizing agency. Thus the main result of a weakening of the intensity of selection is to increase the range of genetic variation. I suggest that it is largely this increased variation which enabled men to adapt themselves, not only to every climate of the world, but to the changes which they made in their own environment. Let me take a simple example, which I am sure is not original, the case of congenital myopia. Natural selection must have prevented it becoming at all common in primitive men. But one or two myopics were an advantage to a small hunting tribe, since, though disqualified for hunting, they alone had fine enough vision of small objects to make needles and arrow heads efficiently. It is not a coincidence that *Wayland Smith* and *Hephaistos* were represented as lame. If a lame man was looked after by his fellows he could, and doubtless often did, make weapons for his tribe. No doubt the human species would have degenerated had there been no selection against lameness. Fragilitas ossium might have become quite common. But it was advantageous that

selection against it should be very much weaker than it is in other bipedal mammals such as kangaroos.

As *Haldane* and *Spurway* [1954] have pointed out, the social insects have all achieved social life by polymorphism, and in particular by exploiting the social utility of individuals which are sterile, and whose individual fitness, or adaptive value, is therefore zero. Human polymorphism is most striking on the psychological level. We do not know whether the psychological polymorphism discovered by *Oettingen-Spielberg* [1949] in hive bees, where only about 5% search for food, while the remainder go where they are directed, has a genetical basis. The social insects have achieved their success in much the same way as man, by instincts which lead them to feed and care for weaker members of their own species (for example bumble bees too weak to gather food, but capable of looking after larvae) and even members of other species.

When it is understood that natural selection acts mainly by diminishing variation and only to a small extent by changing gene frequencies, the question at once arises "What is the optimal level of natural selection for a given character in our species?" This cannot usually be answered. It can be answered for dominant and sex-linked sub-lethals such as haemophilia and epiloia. The answer is that ideally we should like to prolong the lives of abnormals to the normal span, while preventing them from breeding, preferably by persuasion. Similarly we should like to replace the drastic selection against lethal and sublethal autosomal recessives by a much slower eugenic selection against parents known to be heterozygous for numerous such genes (for most people are probably heterozygous for at least one).

It is not so easy to say anything about the desirable level of selection for quantitative characters. We do not know what would be the result of relaxing natural selection for birth weight. If this is largely selection for heterozygosis, the effects might be rather slight. Alternatively the very light and very heavy babies now eliminated at or soon after birth might grow up to unhealthy adults. This could perhaps be determined by following up a group weighed at birth throughout their lives, since it is certain that selection for birth weight is already weaker in many countries than it was a generation ago.

Finally a few words may be said on the immediate future. In hygienically advanced cultures selection by death has been mainly replaced by selection by differences in family size. Except as regards intelligence very little is known as to the correlation of measurable characters with family size, and even this correlation is changing fairly rapidly. Phenotypic

selection is favouring moderately low intelligence and acting against very high and very low intelligence. As *Penrose* [1955] has shown, this is compatible with stabilizing selection, though there is probably some directional selection. Similar data on other measurable characters would be of very great interest.

In conclusion I want to emphasize that we must try to argue from phenotypic to genotypic selection, but that we cannot do so without adequate data. In the first place if any environmental influence simultaneously alters a metrical character and raises fitness there is phenotypic selection in the direction in which the character is altered. Thus if an adequate diet promotes growth in length there is phenotypic selection for length. If education reduces fertility and raises the score in intelligence tests there is phenotypic selection for a low score in these tests. Secondly even if a metrical character is wholly determined genetically, phenotypic and genotypic selection may be in opposite directions. Thus consider a random mating population segregating for a pair of allels G and g, and with the following characteristics:—

Genotype	GG	Gg	gg
Metrical value	A+b	A	A—c
Relative fitness	1—k	1	1—l
Frequency	p^2	2pq	q^2

where $p+q = 1$.

Selection changes the mean of the metrical character from $A+bp^2—cq^2$ to $A+\frac{(1—k)bp^2 — (1—l)cq^2}{1—kp^2—lq^2}$

The selective differential is the difference of these means, or $\frac{(kp^2+lq^2)(bp^2—cq^2) —bkp^2 +clq^2}{1—kp^2 —lq^2}$

The change in gene frequency is

$$\Delta p = \frac{pq(lq—kp)}{1—kp^2—lq^2}$$

If the population is in stable equilibrium, k and l are positive, and $p = \frac{l}{k+l}$, $q = \frac{k}{k+l}$, but the selective differential is $\frac{(c—b)k^2l^2}{(k+l)^2(k+l—kl)}$. This is positive if c exceeds b. That is to say at equilibrium phenotypic selection is in the direction of the more dominant character.

If the population is not in equilibrium, phenotypic and genotypic selection may be in opposite directions. Thus if $p = q = \frac{1}{2}$, $c = 6b$, $k = .2$, $l = .1$, the selective differential is $\frac{b}{148}$, while $\Delta p = \frac{-1}{74}$.

Where many genes are concerned, it is easy to show that some genes may be being selected so as to have a positive effect on any given character, others to have a negative effect, even if selection is wholly based on the values assumed by the character.

It is probable that, when measured over long periods, phenotypic and genotypic selections are almost always in the same direction, but they certainly need not be so over a short period such as three human generations.

To sum up, although we know more about natural selection in man than about natural selection in any other species in its normal environment, we do not yet know very much. I have tried to indicate the need both for more data and for greater precision in our thought.

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THE INTERACTION OF POPULATION CHANGES AND HEREDITY

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The interaction between the size, structure and general conditions of a population on the one hand, and the composition, distribution and actions of the gene-mass on the other, presents a great many difficult problems. Certain aspects of these problems have been discussed by Dr. *Sjögren* in a paper, elaborated in cooperation with me and presented at the World Population Conference in Rome two years ago. (*Torsten Sjögren:* "Probable trends in the distribution of genes affecting the characteristics of the population". This paper is also published in Eugenics Quarterly, Vol. I, No. 4.) At the conference in Rome very interesting contributions to the study of the relation of population changes to the distribution of genetic factors were given by, among others, the President of this congress, Professor *Kemp*, and Drs. *McKeown*, *Penrose*, *Stern*, *Sutter* and *Tabah*, *Falls* and *Neel*.

Especially from the theoretical and methodological view-point important researches in this field have been made, for instance, by Drs. *R. A. Fisher* and *Haldane*. During the last decade many books and papers on the subject have been published by a number of scientists—human-geneticists and others—but obviously it is needless to attempt a survey of this literature here.

However, partly owing to unavoidable complications of many kinds, but not always for this reason, the empirical materials available for analysis and the practical results published do now and then leave a good deal to be desired. The collecting of basic material and the follow-up studies are often expensive and time-consuming. In some countries it is

difficult or impossible to get the necessary genealogical data, to follow migration, and so on. Especially in the socially very important psychiatric field—of the total number of beds in somatic and mental hospitals and asylums in Sweden about one third are occupied by psychotics and more than one fifth by schizophrenics only—there are difficulties in getting reliable information concerning affected persons who have recovered or died many years ago. The complications arising in avoiding bias in the material for study and the problem of evaluating the effects of such bias are often considerable.

Nevertheless practical human genetic research has, not least in its social applications, a series of advantageous premises. In many countries there is a very careful registration of the population far back in time, and as a rule one can get reliable catamnestic data from parish registers, hospital and other medical case-records and also from the affected persons themselves or their relatives. The inhabitants are usually most interested in the exploration of hereditary diseases, and as a rule they cooperate willingly. There exist comprehensive statistics on demographic and medical conditions—births, marriages and divorces, fertility, morbidity, deaths and causes of death. In human genetics one has the opportunity of, and the interest in, studying topics regarding psychic capacity and mental disease, diseases of old age, and the status and changes in advanced age-groups on the whole. The Swedish essayist, Professor *Olle Holmberg*, writes in «Thoughts on venison and other things»:

> Only in youth and the vigour of health can natural life be lived, and animals in nature are young until they die. Man, as soon as he acquired the ability and understanding, withdrew from natural life, raised roof and walls round himself for the nights, invented weapons and shield, and succeeded in exploring the possibility of old age.
>
> Nowadays, old age is much more than a possibility.

These special aspects of human genetics are well-known. They have been discussed in different connections by many authors, and it might thus be considered superfluous to mention them here. However, it ought to be stressed that population changes often strongly influence the conditions for research.

On the highly unrealistic assumption that the circumstances under which a population lives remain unchanged in all relevant exogenous respects, an equilibrium will be successively established in the composition, distribution and actions of the genes. For a certain gene-difference this equilibrium may be stable or unstable, for instance owing to the prevalence of the gene in question and the size and structure of the breeding population. Yet it should be emphasized that it is always a matter of

statistical equilibrium, that is, an average mathematical expectation. A complete equilibrium can arise only in the special case—without interest for the present discussion—that at a certain locus we do not deal with any gene-difference at all, but with a non-mutating gene common to all individuals of the population. In all other instances it holds true that assortative mating, differential fertility, differential mortality, mutations, crossing-overs and chance variations, as well as selective migration, bring about changes in the composition and distribution of the gene-mass which affect the characteristics of the population.

In this genetic play of chance many tens of thousands of gene-differences are involved, and it is then in full agreement with the laws of probability that for many of the genes considerable displacements in the frequencies will occur, and this even if the breeding population is comparatively large. Consequently, in genetic reasoning one must often use other probability-schemes than those generally employed. The problem is further complicated through the material for study frequently being selected *a posteriori*. In other words, it is just those gene-differences in which large chance deviations have occurred during a number of generations that attract attention. Owing to this bias connected with the choice of research-object, the magnitude of the genetic changes—mutation pressure, differential fertility as between dominants and recessives or heterozygotes and homozygotes, selective mortality—is often misjudged. A certain disease may, for instance, have been taken up for study in a certain limited geographic area (possibly of isolate type) precisely for the reason that especially many cases of the disease have been found there. Or one starts with a certain geographic area or a section of the population defined in another way, and then gets one's attention drawn towards such diseases, anomalies, traits, as are, due to chance, more frequent in this group than in others. The material can then be well-suited, or even very well-suited, for elucidating the clinical features of the disease and the mode of inheritance. On the other hand, it is apparent that such a material cannot serve as the basis for determining the mutation pressure, and it cannot be used without great care in the study of differential fertility and excess mortality.

Generally speaking, it is in view of these circumstances justified to state that tests of significance and other statistical criteria must be used with great discrimination in practical human-genetic research.

To be concrete in the following, I have chosen examples from Sweden, as I know Swedish statistics fairly well. However, the conditions are very similar, at least for the most part, in other western countries. In many

respects—regarding geographic and ethnic origin, as well as socially, culturally and economically—the population of Sweden is very homogeneous. It amounts to 7.3 million, and the mean expectation of life at birth is, according to life tables for the period 1946–50, somewhat more than 70 years. In a stationary population of this size and type one should thus have around 100 000 live births a year. Possibly a hundred thousand mutations capable of living occur in such a birth-group. The great majority of these will be eliminated within the next few generations—not through antiselection or differential fertility, but simply because of chance fluctuations. But on the other hand, chance deviations must result in certain of these mutations becoming rather widely dispersed. Dr. *Sjögren* has at this congress given a preliminary report of our study on essential tremor in a north Swedish parish. It is here a question of a monohybrid dominant disease, where only one or at most a few mutations have occurred in more than 300 years, but nevertheless the gene is now present in about 6 per cent of this population or in more than 300 people.

In spite of such examples—many could be cited from the literature—it may be stated that the changes in the composition of the gene-mass in connection with the transfer of genes from one reproducing generation to the next take place very slowly. The time unit is the generation, that is, on an average the father's or mother's age at the child's birth. In the long run, however, these specifically genetic changes will be important.

The main effects over shorter terms originate in the opposite way, inasmuch as changes in the structure and general conditions of the population strongly affect the action of the genes and the composition and distribution of the gene-mass. Especially in social applications of human genetics and in evaluating probable trends must these effects be taken into account, as in many instances they acquire a much greater quantitative significance than do those arising from purely genetic changes. Yet many of these population changes are presumably more or less influenced by genetic differences.

Population changes in modern occidental communities occur rapidly and are of quite another order of magnitude than chance deviations. A short survey of such population factors and some figures from Sweden may be given to elucidate the problem. It should be stressed that it is not here a question of alternatives, but of interactions.

1. Size and geographic and social delimitation of the total and the reproducing population. Especially does one have to take into account the effect of strong increase or decrease in population and of the formation or breaking up of isolates, both geographic and social, for instance owing

Table 1. Population

Population (million)	1900	1950	Increase
Rural	4.0	3.8	—7 %
Urban	1.1	3.3	197 %
Total	5.1	7.1	37 %

to altered facilities for communication, circulation in class status, levelling or other changes in the distribution of income, and so on.—The changes in total population and urbanization are seen in table 1. As in other countries, there has occurred a rapid development in communications, in particular through bus routes and the general evolution of motoring. The significance of this in a country with only 18 inhabitants per square kilometer can hardly be exaggerated. Shortened working hours and statutory holidays for all employees, and the general rise in economic standards as exemplified in table 2 have furthermore contributed to the increased mobility.

Table 2. Income

Personal income	Number of income earners 1953 in relation to number 1945
Income exceeding	
8,000 Sw. Crowns (nominal)	600 %
8,000 Sw. Crowns (in 1945 money value)	270 %

2. Length of life and age-distribution of the population. Of particular interest here is the continual augmentation of the mean expectation of life at different ages, as shown in table 3, and the unavoidable changes in the structure of the age pyramid. Some figures concerning the age-distribution in future years are given in table 4. The population over

Table 3. Mean Expectation of Life, Years

Age	1901–10		1946–50		Increase	
	Men	Women	Men	Women	Men	Women
0	54.5	57.0	69.0	71.6	14.5	14.6
20	45.9	47.7	52.1	53.9	6.2	6.2
50	23.2	24.7	25.0	26.3	1.8	1.6
70	9.8	10.5	10.4	10.9	0.6	0.4

67 years of age in relation to the age-group 18–64 may be expected to increase by 65 per cent from 1950 to 1985, thus in 35 years. This increase is not so much due to reduction in mortality, but is for the most part conditioned by the large variations in birth-rate and the changes in emigration and immigration.

Table 4. Age-distribution

Age-distribution	Persons over 67 years per 1000 persons in age-group 18–64
1950	136
1965	170
1975	202
1985	224
Life table 1946–1950	210

3. Sex-distribution, especially disproportions in marriageable age-groups. Such disproportions arise from variations in birth-rate, if men marry at a later age than women, and to a marked extent from differences between the sexes in respect of migration. The figures in table 5 give an

Table 5. Sex-distribution

Sex-distribution of single, widowed and divorced persons in age-group 20–49 years	Men per 100 women 1940	1950
Agricultural population	222	275
Other population	91	109
Total population	116	131

idea of the existing large discrepancies in the geographical distribution of unmarried people in the age-group 20–49 years (in marriages contracted during the period 1946–50 95 per cent of the men and 87 per cent of the women belonged to this age-group).

4. Marriages. Over a long period the marriage-rate has been very low in Sweden, but during the last two decades, on the contrary, the figure has been extremely high. As seen from table 6, the number of marriages in the period 1901–10 was almost doubled in the period 1941–50, and the

Table 6. Marriages

Marriages	Annual average	Per 1000 mean population
1901–10	32,000	6.0
1911–20		6.3
1921–30		6.5
1931–40		8.2
1941–50	60,000	9.0
1941–45		9.6
1946–50		8.5

marriage-rate increased by 50 per cent. In a stationary population of 7 million with 100 000 births per year, one cannot possibly have more than 50 000 first marriages per year. Taking early deaths and about 10

Table 7. Marriages of Widowed and Divorced Persons, 1941–50.

	Per cent of all marriages	
	1941–45	1946–50
Men	8.4	12.0
Women	5.8	9.0

per cent remarriages into account, the marriage-rate should not exceed 7.5 per thousand inhabitants, but in Sweden it has been higher than this every year from 1934 to 1951, in some single years almost 10 per thousand. —Of the marriages in the period 1941–50, about 10 per cent for men and more than 7 per cent for women were remarriages (compare table 7).— As a consequence of the low marriage-rate in the past, the incidence of single persons in the later age-groups is very high, and this in spite of mortality being lower for the married than for the unmarried. As is seen

Table 8. Single Persons in Different Age-Groups, 1950

Age	Men	Women
50–74	14.2 %	20.7 %
40–49	16.7 %	16.7 %
30–39	23.4 %	15.1 %

from table 8, more than 20 per cent of the women in age-group 50–74 years are single, while in age-group 30–39 years, where marriages are still taking place, the figure is only 15 per cent.—From table 9 is seen

Table 9. Mean Age of Single Persons at Marriage, Years

	Men	Women
1931–40	29.4	26.5
1941–50	28.7	25.8

that the mean age at first marriage is rather high in Sweden. On an average the husband is about three years older than the wife. However, there are great variations as between different parts of the country and different groups (age, occupation, etc.). — Divorces have increased heavily —table 10—and in 1954 amounted to 16 per cent of the number of

Tabe 10. Divorces (Number, Annual Average).

1901–10	500
1921–30	1,800
1931–40	2,900
1941–50	6,100
1954	8,700

marriages contracted in the same year. Of the divorces almost half take place during the first ten years of marriage, and about two thirds occur in marriages where there are children.—The geographical correlation between husband and wife as regards birthplace, and residence at marriage, is much less nowadays than formerly.—The incidence of consanguineous marriages has diminished for two reasons, namely urbanization and increased mobility of population, and reduction in the average size of family.

Table 11. Live Births (Number, Annual Average).

1901–10	137,000	1909	140,000
1911–20	126,000	1919	115,000
1921–30	106,000	1020	139,000
1931–40	90,000	1924	109,000
1941–45	122,000	1934	85,000
1946–50	125,000	1944	135,000
		1954	105,000

5. Fertility and birth-rate. Of particular importance here are age at reproduction and distribution according to the number of children—physiological fecundity, sterility, voluntary limitation of the size of family—and, further, social and geographic differences and time variations in fertility, the mother's age at childbirth, and the number of children.—The absolute number of live births is shown in table 11. I think the most adequate adjective to describe the changes is immense. The variations are the result of a very complicated interaction of events and attitudes. Only to mention a few factors, I should like to call attention to the reduction in birth-rate up to 1935 being partly conditioned by the successive urbanization and the adoption of voluntary birth-control. To this should be added, as a characteristic feature for Sweden, the very low marriage-rate and a comparatively large number of childless marriages during that period. As is seen from table 12, in 1935 more than 17 per

Table 12. Children in Existing Marriages; Wife over 45 Years of Age, 1935

Number of children	Per cent of marriages
0	17.5
1	14.4
2	17.2
3–4	25.6
5–6	13.4
7–8	7.1
9–	4.8
	100.0

cent of all existing marriages where the wife was over 45 years of age were childless, and in another 32 per cent the number of children was only one or two. The large number of births during the forties was above all conditioned by the marked increase in marriage-rate far beyond the maximum level in a population in equilibrium.— It is rather typical for demographic changes of this kind that they, so to speak, exaggerate what really happens. To clarify this, I may give the following simplified hypothetical example. Suppose that in a population group a strict 4-child system has been practised for a long time, with two children born when the mother was between 20 and 29 years and two when she was between 30 and 39. Suppose then that this population suddenly adopts a 2-child system, where two children are born when the mother is between 30 and 39. The final result of this change will naturally be that the birth-rate drops to something less than half or, if we leave out the effect of mortality in the age-interval 20–39, to exactly half. But, obviously, the short term effect will be that the birth-rate drops to nil. Those women who are over 30 already have their two children and therefore stop reproduction. Those women who are under 30 will postpone having children until after they have reached the age of 30 years.—In fact it is mechanisms of this kind, though of course not so extreme as the example, that lie behind a good many of the variations in birth-rate.—In a limited period of time there are important differences in birth-rate and fertility as between different geographic areas and different social groups. However, it is often the case that differences of this kind exist chiefly as a result of time-lag. In most countries voluntary birth-control has been introduced earlier in the socially, economically and educationally higher levels. But it is far from certain that such differences as are to be found for a limited period will continue to exist for any length of time, or will bring about any far-reaching effect on the composition of the gene-mass in generations to come. Presumably, voluntary birth-control has indeed entailed a certain antiselection from a purely genetic aspect. On the other hand, it must not be forgotten that this control has surely been of importance to the general rise in standards, and to a certain extent formed the basis for progress in social welfare and medical resources.—Net reproduction rates and similar comprehensive statistical measures based on the conditions in different age-classes during a limited period will evidently often be misleading and must thus be used with the utmost care in human genetics. To a certain extent the same is valid also concerning statistics on, for instance, the average number of children per family, the distribution according to number of children, and the fertility in different age-groups.

—An important factor in the evaluation of trends is the mother's age at childbirth. If there is deficit in reproduction, the loss will be relatively smaller when age on reproduction is high. This, too, suggests caution in using net reproduction rates and in evaluating statistical data on differential fertility.—In Swedish statistics around 10 per cent of all childbirths are registered as illegitimate. However, in many cases the parents marry somewhat later, and in others it is a question of a conjugal association, though without wedding. It would thus be appropriate to state, that the marriage figures are somewhat too low, when seen from a biological and not a legal point of view.

6. Migration, especially selective influx and removals. There was much emigration from Sweden during a long period before the first World War, but in recent years immigration has been in excess—table 13.—As regards

Table 13. Emigrants and Immigrants

Excess of immigrants	Annual average	Per 100 live births in the same period
1880–1910	—22,000	—16
1941–1950	+20,000	+16

internal migration it may be mentioned, that in 1953 5.5 per cent of the inhabitants moved from one community to another.—An idea of recent changes in occupational structure in part connected with internal migration is given in table 14; in only ten years the agricultural popu-

Table 14. Occupation

Population (million)	1940	1950	Increase
Agricultural	2.03	1.65	—19 %
Other	4.34	5.39	+24 %

lation decreased by 19 per cent.—Removals from the rural districts to towns and other built-up areas take place on an average at a much earlier age for women than for men.—Another type of selective migration is that in which oligophrenics are very stationary as to residence—one of the reasons for the higher incidence of oligophrenia in rural as compared with urban districts.

7. Morbidity and mortality within different groups of the population. Important changes in the malignity of diseases have been caused by, for instance, altered resistance or immunity conditions, medical advances, and the introduction of new prophylactic and therapeutic measures. One need

not go further back than one or two generations to reach a time, when conditions of life and death were completely different from those obtaining nowadays. The changes that have occurred and are going on at an ever-increasing rate will cause radical displacement in positive or negative selection that has existed unchanged for centuries.—It is above all infant mortality and mortality in the younger ages that have been reduced. As is seen from the figures in table 3, the decrease in mortality in advanced ages has been comparatively small. This has the effect that diseases of old age—not least those genetically conditioned—become successively more preponderant, both as regards the need for medical resources and as regards the possibility for scientific research.—The high infant mortality in the past was, to a quite dominating extent, caused by exogenous factors, but the differences as between, for instance, urban and rural districts or different social groups may nevertheless have had a genetically selective effect, particularly during periods of heavy increase in population.

8. Advances in human-genetic science. This is a matter of skill, training and so on, but it is also a matter of economy. Money for research is rather scarce, and should therefore be used well. For instance, I do not think it motivated in population studies of twins to invest a lot of money in securing complete exactitude as regards zygosity. Suppose that we have a certain percentage of incorrect statements. Through ordinary methods we can evaluate differences and their statistical significance. We then underestimate the real differences and overestimate their variances. If necessary, one can make due allowance for this bias through a closer study of a sample of the twins. But in view of many other biasses involved —as to reliability of diagnosis, environmental factors, etc.—even this is often superfluous. As a rule planning—*i.e.* utilizing present knowledge —pays very well.

9. Public health. As illustrations may be mentioned prophylactic measures (vaccination etc.), arrangements for the early diagnosing of disease (for instance tuberculosis examinations), regular health control for employees, social medical facilities, advice on abortion, changes in the resources for sick-care and in treatment policy.

10. Social, occupational and economic conditions. Many of these conditions are interrelated to demographic data. It has been the opinion of many that marriages and births can be stimulated through social welfare and tax policy. On the other hand, the housing shortage after the second World War has detrimentally affected the forming of families and the birth-rate.

11. Legislation. For instance, immigration may be regulated. There may exist prohibition against marriage for persons afflicted with certain diseases (as in Sweden for the mentally deficient and mentally diseased) or as to certain degrees of consanguinity. And there may be laws concerning obligatory schooling and institutional care, and, in some quarters, sterilization.

12. Changed knowledge within the population about the heredity of certain diseases. For example, this may bring about effects as regards marriage and reproduction, and change assortative mating and the incidence of consanguineous marriages.

13. Disturbances of the normal development. As examples may be mentioned radioactivity—this does not only influence the mutation rate, but can also affect several population factors and thus, indirectly, the gene-mass—and, furthermore, variations in climate, war, and natural catastrophes.

Data regarding population, vital statistics, mental disorders and suicide are given in an investigation by Dr. *Sjögren* and myself. (*Tage Larsson* and *Torsten Sjögren:* "A methodological, psychiatric and statistical study of a large Swedish rural population"—(Acta psych. et neurol. Scand., suppl. 89, Copenhagen 1954). There we also deal with methods and selective factors in population studies, the morbidity-risks for psychoses and oligophrenia in the general population, and excess mortality and probable trends regarding these diseases. Some comprehensive figures are given in tables 15–18.

Table 15. Patients and First Admissions at Mental Hospitals

Average annual number in thousands	Patients	First admissions
1911–15	9.0	1.8
1926–30	14.1	2.6
1946–50	34.0	7.4
Schizophrenics in relation to all psychotics:		
1931–35	75 %	43 %
1941–45	72 %	32 %

Table 16. Marital Status for the Mentally Diseased and Mentally Deficient, 1030. Observed Percentage of Single Persons and Expected Figure (according to marital status in different age-groups in the general population).

		Observed	Expected
Mentally diseased	Men	77	28
	Women	65	27
Mentally diseased and	Men	87	41
mentally deficient	Women	77	37

Table 17. Morbidity-Risks and Excess Mortality for Psychotics (affected and previously affected) and Oligophrenics.

Main diagnosis	Aggregate morbidity-risk up to 80 years of age, %		Remaining mean expectation of life compared with that for general population, %	
	Men	Women	Men	Women
Psychosis:				
All forms	4.7	5.7	71	67
Schizophrenia	1.6	1.6	72	63
Manic-depressive	0.9	1.2	95	91
Senile	0.6	0.8	50	60
Presenile	0.7	1.0	60	67
Low-grade oligophrenia	1.0	0.75	70	70

Table 18. Number of Psychotics (affected and previously affected) and Oligophrenics, thousands. Estimations based on present morbidity-risks and excess mortality.

	1945	1965	Increase (round figures)
Psychosis:			
All forms	90	108	20 %
Schizophrenia	39	44	13 %
Manic-depressive	22	27	25 %
Senile and presenile	9	13	50 %
Low-grade oligophrenia			
Total	35	39	10 %
Age-group 7–16 years	7	10	40 %

Time does not allow more than some rather short comments and conclusions on the basis of this list, which is of course far from complete.

For several demographic reasons, among others the large increase in population during recent centuries and the increased mobility, there has been a reduced margin for the play of chance as regards the common genes and the manifestation of the rare recessive genes. Over a long period the decrease in consanguineous marriages and the greater geographical freedom in the choice of marriage partner will reduce the manifestation of malignant recessive genes.

The strong reduction in infant mortality and mortality in general has caused the genetically conditioned diseases to acquire a more and more prominent place in medicine. Especially does this apply to dominant diseases with late manifestation and, not least in respect of their importance socially and from the viewpoint of sick-care, such diseases as, for instance, schizophrenia, diabetes, senile psychoses, oligophrenia.

Geriatric genetics will, within the near future, become a most

important field of research. In the case of the Swedish population this universal problem is accentuated by the abnormal age-distribution.

In Sweden, as in many other occidental countries, the marriage-rate has increased during the last few decades. The prevalence of childless persons has diminished, and at the same time the dispersion of family size has contracted. In other words, the number of sibships is greater, but on an average they are smaller than previously. The reduced number of individuals without children, and the reduced number of children per family with children make the hypothesis of panmixia less unrealistic. Increased migration and increased incidence of divorce act in the same direction.

Although the number of children per family has decreased, and in spite of the positive correlation between sibs in respect of length of life, the improvements in mortality will have the consequence that in family investigations the sibships in advanced age-groups will be larger than was formerly the case. Further, considerably more adult twin pairs will be available for investigation. In the study of dominant genes, even if the age of manifestation is rather high, it will be an advantage that in a great many instances both parents will be alive. As to diseases with early onset, both parents and all the grandparents will often be available. Diseases with a relatively late age of manifestation have frequently caused difficulties for the reason that parents and grandparents, or some of them, have died before the manifestation age.

The study of rare recessive diseases with early manifestation will become more difficult. Hitherto, the criteria mostly used have been analysis of pedigrees, calculations concerning the incidence of consanguineous marriages, and estimation of the *Mendel*ian ratio in families with at least two children (with due corrections for the method of sampling). As time goes on, these methods will become less useful, since—in the case of reduced isolation, smaller number of children in the families and decreasing incidence of consanguineous marriages—they will require very large materials. The classical methods for family investigations must thus be supplemented, new methods for the collecting of material introduced and the analysis sharpened. Possibilities for the pooling of material obtained by different researchers ought to be created. In unbiassed samples (or, more generally, in samples where biasses can be evaluated) comparisons with the conditions in the general population might be employed. For instance, families with only one child can be used in the analysis if the general distribution of the population according to family size is known.

An interesting example of new paths is Dr. *Alström*'s study of retinopathy, where the starting-point was blindness with obscure diagnosis, but in a great number of cases this could be made through genetic analysis.

The increased length of life and the greater mobility of the population may entail essential changes regarding assortative mating.

Selective migration gives rise to special problems in population studies, for instance the necessity of using birth population and not resident population in genetic analysis. In reviewing materials of dominant diseases with rather late onset one is often astonished that skipping owing to a parent's death before the age of manifestation is found only on rare occasions. In fact, this is often due to selective migration; if the parents die early, the probability that the children will move away increases. Furthermore, the early death of a parent may be the reason for twins being reared apart, and thus imply a bias.

The lack of geographic balance in sex-distribution in marriageable age-groups creates an entirely new type of antiselection. It is of great significance that the genetic aspects of this problem be given sufficient attention.

Voluntary birth-control lessens the importance of biologically conditioned differential fertility. This may cause considerable changes in genetic selection.

The breaking up of isolates and the reduction of consanguineous marriages bring about a change in the distribution of the gene-mass with increased heterozygotization and thus—possibly—altered selection. Nevertheless, because of the higher marriage-rate and the reduction of family size it is to be expected—other factors being equal—that the new generation will become more like the present one with regard to the composition of the gene-mass than was formerly the case in two successive generations.

The continually increasing urbanization and industrialization, as also changes in medical resources and treatment policy, strongly influence the need for and the possibilities of sick-care. In many respects the consequence of this is also a changed social malignity of diseases. As has previously been discussed at some length by Dr. *Sjögren* and myself, in oligophrenia the changes of the social and economic conditions bring about an increased malignity. Thanks to the opportunities of employing different groups of partially incapacitated people that exist in a highly specialized industrial society, diseases affecting the capacity of physical action, deafness and the like, are often less socially malignant nowadays than formerly.

Determinations of morbidity-risks in the general population acquire added importance, both from the epidemiological point of view and as the basis for correlation studies (analysis of coincidence). This analysis is becoming a valuable research-method in human genetics.

In morbid changes of various etiology the crude clinical picture may be quite similar. Through biochemical and detailed clinical studies of genetic entities the possibilities of elucidating the biochemical abnormalities and the normal processes in metabolism will be increased. Therefore, even very rare genetically conditioned diseases and anomalies will come to be of great interest. The ways of securing knowledge about such diseases and anomalies will in part, owing to population changes, be other than previously.

Altogether, population changes affect not only the actions of the genes and the composition and distribution of the gene-mass, but also strongly influence the scope, topics and methods of human-genetic research.

Developments more than ever necessitate collaboration between researchers. It is thus an urgent desideratum that the material be so published that others can use it, for instance with other analytic methods, for the pooling of material, comparisons, coincidence analysis, differential diagnosis, etc.

In planning and carrying out human-genetic and epidemiological studies due attention should be given to demographic data and their changes. Particularly should this be stressed as regards the social applications of human genetics.

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CHANGING PATTERNS OF SELECTION

By R. C. COOK

Over the past half century, genetic research has solved one of the enigmas which perplexed post-Darwin evolutionists, namely why does the adoption of a parasitic role by a species almost universally result in the loss of organs no longer required for survival? This phenomenon seemed to invite a *Lamarck*ian explanation. "Use" having ceased, the stimulus to the maintenance of the organ disappeared, and the organ withered orthogenetically. The trouble with this idea is that it lacked any experimental support. Yet no alternative explanation was immediately forthcoming. Genetic theory has now reached the point where a more realistic explanation of this phenomenon is possible. This explanation involves the nature of the mutation process, and is fully congruent with the established experimental and observational facts of genetics. It has been elaborated by *Muller*, *Beadle*, and others.

The phenomenon of mutation has been widely studied in many organisms. The results are consistent: that mutations at all loci occur at a low rate—the rate varying for different loci. These mutations are at random—and in many directions. The great majority are lethal, many of the rest are non-adaptive, and only the rare mutation is of a nature to add to adaptive fitness. Mutations are conceived of as being biochemical changes in a very complex system, highly integrated and timed to trigger a developmental or metabolic sequence.

The development of organic adaptation then becomes a problem of scanning and screening the mutative changes which are constantly appearing in any species.

The scanning process consists of sexual reproduction, with meiosis—including crossing over—and the recombination of all possible combinations of gametes in fertilization. The varied genotypic combinations are

screened by the test of survival. The screening process has been accomplished by selection. In the main, this has consisted of the ability of the organism to survive to reproduce.

Dr. *R.A. Fisher* has described sexual reproduction and the mutation process as a remarkable mechanism for generating very high degrees of improbability. By this he means that the rare adaptive mutation is scanned in varied genotypic contexts, screened by selection, and recombined by sexual reproduction with other rare adaptive mutations. Since the vast majority of mutations are non-adaptive, any breakdown in the scanning and screening apparatus is inevitably bound to result in a build-up of non-adaptive mutations and in an inevitable loss of adaptive fitness.

The genetic explanation of the adverse influence of parasitism on organic systems is thus seen to be the result of a breakdown of the screening process, which will inevitably bring about an accumulation of non-adaptive mutations.

It follows that parasitism *per se* is not the "cause" of the loss of adaptive fitness. Rather it is the breakdown of the screening mechanism which parasitism brings about makes such loss inevitable through the build-up of non-adaptive mutations. Any situation which results in the breakdown of the screening mechanism would be expected to have this same effect, regardless of whether the life habits of the organism might be considered "parasitic" in a conventional sense or not.

Until very recently (on a geological time scale) it would appear that the scanning-screening process has applied to man in much the same manner as it has applied to any other species in being. The extent to which the evolution of the uniquely human innovation of culture, with the development of the arts and sciences, has affected the screening process is certainly a matter requiring further investigation. Dr. *Haldane*, it appears, is of the opinion that the selective screening has been limited for several thousand years to resistance to infectious diseases. One is tempted to wonder whether this may not be a considerable over-simplification. One suspects that some who are participating here would concur in this speaker's doubts. Whether or not this the case could be a matter of the utmost importance to man in the generations to come. If *Haldane* is right, then the above analogy to parasitism may not apply even with the revolutionary changes in survival which have occurred during the first century of what was described by the late *Norman Himes* as "the Vital Revolution". If *Haldane*'s assumption that there has been no selective screening of non-adaptive mutations for several thousand years is wrong, it invites conclusions which might lead to the most serious consequences.

For this is the crux of our problem. The screening by the test of survival to reproduce necessarily implies that the non-survivors, the non-adapted for most varied reasons, do indeed carry with them enough of the ever-recurring non-adaptive mutations to maintain the genic balance of the species.

The question of how much pre-puberty mortality would be required to maintain such a balance has been given some consideration in recent years. Dr. *Muller* explored the question of the balance between "fitness" and non-adaptive mutation this morning. Elsewhere he has estimated that 20 per cent of pre-puberty mortality would be necessary to keep non-adaptive mutations at the existing level. Until very recently, and in all human cultures most of the time, at least half the babies born have failed to reach maturity. If less than half these early deaths were selective by reason of mutational disability in the sense used by *Muller*, the fitness balance would have been maintained. Even granting that a great deal of the high mortality from infections diseases were non-selective, there appears to be a considerable margin to permit the screening for other adaptive qualities.

Developments since about 1800 have wholly altered this picture. The successful attacks on the mass killers which have plagued mankind for many millenia have mainly been effective on early deaths. In those countries which have fully exploited the modern death-deferring techniques, pre-puberty mortality has literally been decimated. In the countries of Northern and Western Europe and in North America it is as low as 5 per cent. Obviously, screening by death selection can no longer be effective. In the unlikely contingency that all pre-puberty deaths where selective, these would be only about a quarter of the number that *Muller* considers necessary to eliminate the ever-recurring non-adaptive mutations.

Whatever may have been the selective forces acting on the gene-pool of the human species during its evolution up to now, the revolutionary change in the pattern of mortality which is even now spreading over the world has drastically altered this pattern. The analogy to the situation when a parasitic habit of life is adopted is obvious and startling. Unless the human species has some built-in mechanism unknown at this time to genetics, steady accretion of morbid mutations in the gene-pool of the species seems inevitable. The recent tendency to increase the radioactivity of the human environment ominously accelerates this trend.

The only other escape from this dilemma would be to be able to reassure ourselves that in the modern world birth selection had somehow supplanted death selection. Most of the evidence suggests that in the cumu-

lative effect current reproductive patterns tend toward being non-adaptive. For example:

1. The birth differentials which exist in modern industrial cultures do not appear to be adaptive. The groups which show the lowest reproduction tend to contain a high proportion of individuals whose abundant reproduction would seem to foster adaptive advance.

2. The discovery by *Reed* and *Palm* that in families carrying the dominant gene for *Huntington*'s chorea, the carriers of the gene had a much higher fertility than their siblings who did not carry the gene.

3. The recent announcement of Dr. *Alan Guttmacher* and associates—guardedly enthusiastic in tone—that a diabetic woman had survived her fifth pregnancy underlines the fact that reproduction of known carriers of genetic defect has to a certain extent been facilitated during the vital revolution. Dr. *Guttmacher* commented on its rather bizarre genetic implications. One notes a tendency in certain quarters to look upon the joys of reproduction as compensating for deprivations and deficiencies in other aspects of the life experience. The same trend was recognized by the preceding speaker, Dr. *Aschner*, on the basis of a far larger sample.

These items are cited as no more than straws in a wind which seems to be blowing mostly and strongly in one direction.

A recent survey by The United Nations of the extent and causes of pre-natal and neonatal mortality, emphasized a parallel trend. In the analysis of the causes of pre-natal and post-natal mortality, the work of the staff of the National Institute of Demography in Paris was featured. This stressed the distinction between endogenous and exogenous deaths. The former are mainly limited to the last days of pregnancy and to the first days of life. They are considered to be to a considerable extent due to genetic causes. Until the present time, the attack on infant mortality, strikingly effective in respect to exogenous causes, has had very little effect on endogenous deaths. Even in the more advanced countries, infant deaths during the first day of life, have not greatly changed over the past generation.

The proposal to mount an intensive attack on the endogenous deaths has an undoubted and unanswerable humanitarian and sentimental appeal. So has any program to ease the afflictions of those unfortunates who later in development suffer genetic defects, deficiencies and malformations. Nor is there any reason why these things should not be done. It cannot be emphasized too strongly that, from the point of view of the scanning and screening process, the crucial question is not survival, but reproduction.

This brings us to the next and unwritten chapter of our story.

It appears that through the genius of our species we have been able to demolish, in the pursuit of other more obvious goals, the screening mechanism which over previous ages has maintained our organic fitness.

If further investigation confirms the thesis that decline in adaptiveness is inevitable, then we are confronted by three alternatives:

1. To pretend that nothing has happened, and to let the inevitable take its course. After all what did posterity ever do for us ?

2. To throw away all our modern gadgets and new knowledge, and get back to the "good old days". It may happen in spite of us if we are too prodigal with the abundance of the earth, and too quick on the atomic triggers.

3. To recognize that the Vital Revolution, bringing the power to defer death, and to do away with the tragic futility of half of birth's being wasted, does indeed mark a break-through to a new level of social evolution. How this new venture will end will depend crucially and centrally on human genetics. To make the future safe over any long pull, clearly ways must found to substitute birth selection for death selection.

To comment that this is one of the most tremendous, nay terrifying items ever put on the agenda of the human species is an understatement. The alternatives being what they are, it will be difficult to dodge the issue, or to turn back. Yet the difficulties are enormous. So many very ancient, very deep and very sacred ideas will have to be re-examined. In a sense, what the emergence of genetics and of human genetics especially has given medicine is an new dimension : time.

If there is any validity in the analogy to paracitism, it would seem that the fate of posterity over the long pull cannot safely be left to the biochemists and the physiologists with pills and syringes.

To some geneticists eugenics is still a naughty word and quite understandably. The idea of tinkering at this level with human lives is dynamite. But the basic concept, namely the enhancement of the inborn qualities of future generations of human beings remains sound. What some eugenists forget was that this has to be brought about in a social context. Some took naive, even dangerous views of how this might be achieved. The enhancement must be voluntary. It calls for some new and very searching re-appraisals of our attitude towards reproduction. Such considerations lie outside the scope of human genetics, being in the fields of social invention, cybernetics and the arts rather than of science.

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CHANGING DEMOGRAPHIC TRENDS OF INTEREST TO POPULATION GENETICS

By F. OSBORN

In the complex social life of man, many factors combine to make the actual redistribution of genes from one generation to another depart widely from the theoretical framework of population genetics. The relative importance of each of these factors is changing rapidly under the influence of changing demographic trends. A brief survey of this situation may be appropriate to a Congress of Human Genetics.

Probably the major forces affecting the distribution of genes from one generation to another in human populations are:

1. Differentials in deaths.
2. Differentials in births.
3. Mate selection.
4. Size of isolates within which people marry.

Each one of these factors has probably played some part in the evolution of life since the beginning of sexual reproduction. Over long periods of time, and until very recently, there was probably not much variation in their relative contributions except as changing size may have varied the effects of isolates. In part of Africa today the interplay of these forces may be much the same as it has been in all past times. But in the larger communities in all of the rest of the world, these forms are being modified by demographic changes which, developing first in the most industrialized countries, are now rapidly spreading over the whole world.

Decline in the Genetic Selectivity of Deaths

The most drastic change has been in the reduction of deaths. In all previous times, the average span of life had fluctuated between 25 and

40 years. More than half of the children born alive died before reaching the mid-term of their reproductive period. In the United States at the time of the founding of the Republic, only 36% survived to age 35[1]. During all man's past, indeed during the whole period of mammalian development, genetic factors relating to survival had a large area of deaths within which they could operate. Differentials in deaths were probably the major factors in selection.

We need hardly recount here the rapidity with which the change to a low death rate has taken place. In the countries of Western Europe and those which have grown up under Western influence, the average span of life is currently over 68 years for men and over 70 for women. 95% of children born alive will survive to reach their reproductive years. In the rest of the world, improvements in public health, water supply and control of malaria and similar diseases are bringing down the death rate with startling rapidity. The death rate in the Soviet Union is estimated at 8.9 for 1953. For Japan. 8.2 in 1954. For Egypt, 17. 8. in 1952. In Ceylon the death rate which in 1946 stood at 20.3 per thousand was reduced by relatively inexpensive public health measures to 10. 4. per thousand in 1954[1].

It is possible that overpopulation and slowness of resource development may move the world back to the old rates of mortality. In such a regression the ranks of the human geneticists would also be decimated and their own problems might overshadow their interest in problems of selection. For our present purposes we may take a more optimistic position, and base our speculations of the future on death rates so low that they leave little room for genetic selection.

There is only one area in which deaths may still be highly selective. In the United States, in 1953, about 67 000 liveborn children died before they were one week old—twice the number of deaths occurring among children in the broad age range from one through 14 years [2]. This represented a reduction of one-third since 1940. But there was almost twice as great a reduction in deaths taking place in later childhood. The hard core of deaths in the first week of life may be largely caused by genetic influences. One third of such deaths are reported under the head of immaturity, and over ten percent under congenital malformations. In any event, the proportion of deaths is small compared to the millions of births taking place in the United States each year. In later childhood, accidents account for a large proportion of the deaths, in certain age groups

[1] Estimated from *Wigglesworth* Table published in American Academy of Arts and Sciences, *Memoirs 2*, Part 1, p. 133, 1793.

for half or more. We seem forced to the conclusion that when rates of mortality are low, the influence of death is chiefly to eliminate genes causing early defects, and that death has little or no effect on the distribution of genes underlying intelligence or personality.

Probable Decline in the Genetic Selectivity of Births

In the United States with a low birth rate, average size of completed family was 3.0 for mothers born 1905 through 1909, and who now, at ages 45 to 50, have completed their childbearing. This compares with average size of completed family in the U.S. for mothers born 1875–1879 of 4.33 children. The proportion of families of various sizes in these groups was as follows [3]:

Proportion of Families of Various Sizes in the United States for Mothers born 1875–79 and 1905-09.

Table 1

	Percent distribution of mothers by number of children ever born		Total children per 100 mothers		Percent of all children	
	1875–79	1905–09	1875–79	1905–09	1875–79	1905–09
Total	100	100			100	100
1 child	15	24	15	24	3	8
2 children	19	29	38	58	9	19
3 children	15	18	45	54	10	18
4 children	13	11	52	44	12	15
5 children	9	6	45	30	10	10
6 or more children	29	12	238	90	56	30
Total children per 100 mothers			433	300		

In groups with exceedingly low birth rates, variations in size of family are even further reduced.

A considerable part of the world's population, perhaps twenty percent, now has a low birth rate and a small proportion of families of five or more children. It has been quite fully demonstrated that the reduction in births has been due to the acceptance of family planning and the use of some form of contraception, and there is little doubt that the same influences are now reducing the birth rate and the proportion of large families in the rest of the world.

In the United States and in most European countries differentials in births between socio-economic classes and between rural and urban groups have in the past always favored the lower class and the rural group. The introduction of family planning and contraception undoubt-

edly widened these differences. *Notestein* [4] reports that among English women who married between 1851 and 1861, fertility and socio-economic status were inversely related, though the differences between the classes were small. But for English women who married between 1886 and 1891, the spread of the classes was more than $2\frac{1}{2}$ times that for the earlier groups.

As the use of contraception becomes more general, these differentials tend to narrow. In the upsurge of births which has taken place in the United States since the war, the increase has been mainly among the urban and the white collar groups who were having the fewest children before the war, while in the rural farm groups the decline in births has continued [5].

In a number of recent studies there is evidence that among groups in which all couples practice birth control effectively, the usual negative correlation between income and size of family is reversed, and people with the highest incomes have the most children and those with the least incomes the fewest children.

Socio-economic and rural urban differentials in births appear to go through three phases. In the first, which continued until towards the end of the nineteenth century, there is no general use of contraception and the differentials are not large. In the second, contraception has spread unevenly, through only the upper part of the population, and the differentials are very large. In the final phase the practice of contraception spreads through the whole population, but with a varying effectiveness, and the differentials are narrowed, and would possibly disappear or even be reserved if methods of contraception should become entirely effective [6].

Whatever the genetic effects of differences in birth rates between the upper and the lower socio-economic groups, we have grounds for believing that extreme differences of this sort are a somewhat temporary phenomenon. Minor differences between these groups might easily be offset by differences in size of family between couples within each group. We know very definitely that family stocks differ in their genetic make-up; we have very little information on genetic differences between the average of any two population groups. There are "superior" family stocks scattered throughout the whole population; we have yet to learn whether they are concentrated in particular areas or among particular groups of people. "Genetic superiority" can only be determined by comparisons between individuals in similar environments.

If present trends continue, we must expect that we are rapidly

coming to a time when families of eight or ten children will be exceedingly rare, and families of twenty almost unknown. The range of variations in size of family is being everywhere reduced, and with this reduction there is a reduction of the area within which variations in births can effect genetic selection.

The degree of genetic selection which could be provided in a group with a birth rate so low as to be at or near replacement will depend on whether births are concentrated in the two or three child families, or whether there is a considerable proportion of childlessness at one end of the scale and of families of four or more at the other end. It is conceivable that a population with a birth rate only slightly above replacement might have a distribution of births providing considerable room for selection, as shown by the following table [7]:

Table 2

Percent of Families of Different Sizes		Total Children		Percent of All Children
19	0 children	0		0.0
15	1 child	15		6.0
16	2 children	32		12.8
18	3 children	54		21.6
18	4 children	72		28.8
14	5 ½ children	77		30.8
100	Grand total	250	children per 100 married women	100

Thus at the low birth rates required for the stabilizing of the world's population, there may still be room for births to be an effective agent of selection, providing families of different sizes differ in their genetic qualities.

It is easy to theorize as to the genetic qualities of families of different size in either high birth rate or low birth rate population groups, but there is almost no real evidence on the subject. Differences in weight and other physical measures between children of different birth order are properly attributable to differences in the environment: and even the known average lower test-intelligence of children in large families is increasingly considered to be the result of the psychological environment. We can hope that before long demographers will begin to fill in some of these gaps in our knowledge. In a large study now being planned in the United States, an attempt will be made to relate physical health, personality traits and traits of intelligence to variations in size of family in large urban and suburban groups.

Mate Selection and the Break-Up of Isolates

One of the striking results of modern communication and transportation has been the enlargement of the local community in which people move about and within which they must of necessity choose their mates.

The work of *Jean Sutter*, and of *Sutter* and *Leon Tabah*, has provided critical information on recent changes in the size of isolates [8]. In the French Département of Loir-et-Cher, the proportion of consanguinous marriages (used as a measure of isolates) rose irregularly from 2% to 3% from 1824 till just before 1900, when it reached 4% or more. After a drop to 1914, it rose again to 4% in 1919 under the influence of the war and has since dropped regularly till in 1950–54 it stood at between .5% and .3%.

The corresponding figures for the Département of Finistère are available beginning with 1911; they show almost identical changes. In terms of the size of the isolates, that is the number of people among whom a mate might be chosen, *Sutter* and *Tabah* have made the following estimates:

Loir-et-Cher . . .	1919–25	270 persons;	1944–53	810 persons;
Finistère	1919–25	1061 persons;	1944–53	2122 persons.

It seems a fair presumption that similar changes have been taking place in all of the countries undergoing industrialization. The effect of the changes on the distribution of genes for defect will be evident to geneticists. Other aspects may also deserve consideration.

In the small isolates in which man's past evolution has taken place, selection must have been due to chance, to genetic drift, or to particular individual characteristics making for survival. Mate selection might play some part in the concentration of certain physical characteristics, and certain broad characteristics of personality, but would have little opportunity to operate on more subtle variants, such as music appreciation, scholarship, interests in art or science.

It is of interest to speculate whether the so-called break-up of isolates may not in effect be a change from a system of geographical isolates to a new system of what might be called psychological isolates. The fact that people live in a large community such as a modern city, does not mean that the entire community constitutes the group within which they may marry. Young people tend quite early to begin to sort out for themselves a group of individuals with interests similar to their own, within which they are likely to marry, and thus the boundaries of the different cultural and psychological isolates keep being more clearly redefined from one

generation to another. Such isolates may in actual practice be no larger than the geographical isolates which they have succeeded. They will not be influenced by chance or genetic drift, but they may be even more effective than the old in bringing about a greater diversity of human interests and abilities, each type concentrated in particular intermarrying groups. All this is at present pure speculation. But it may be well for the geneticist to have in mind that the break-up of the geographical isolates may have an unexpected significance. Taken in connection with the falling off of death selection and the new importance of birth selection, it may be that evolution is entering a new phase in which the distribution of traits of intelligence and of personality may change more rapidly than they have in the past, and in which they will move towards a greater diversity.

Conclusions

The industrial revolution, with is accompaniments of improved communication and transportation, and higher levels of education and economic wellbeing, is bringing about major changes in demographic trends. These changes have taken place first in the more advanced countries, and appear to be spreading rapidly into other areas.

The first change is an increase in the average expectation of life from the old levels which ranged from twenty-five or forty years to the recent achievement of sixty-eight or seventy years. At the shorter span, death prevents some fifty percent of the reproduction of individuals: with the longer span of life, death cuts off only $6\frac{1}{2}$ percent of individual reproduction. Death then effects a selection only of seriously defective genes: it no longer operates to effect a selection of the genes which underlie man's higher qualities.

The second change is a reduction of size of family among individual couples. The proportion of families of five or more is greatly reduced, thus reducing the area within which births may operate as factors for selection. But differences in size of family are still sufficient to be highly selective if different size families have markedly different characteristics.

Finally there is a change towards the breaking up of geographical isolates, thus apparently enlarging the size of the group within which individuals may find their mates. But this may mean that as a result of larger opportunities for selection of mates who are similar in characteristics of personality and intelligence, there is an increasing differentiation into groups each marked by similarity of the individuals of which it is composed.

In each of these areas of change, the conditions surrounding human populations differ markedly from the conditions set up for the theoretical structure of population genetics. What is actually happening in the redistribution of genes from one generation to another can only be determined by research from which the geneticist will determine the relationship of genetic factors to specific measurable characteristics, and the demographer will determine trends in reproduction and survival of people of different characteristics. We have as yet hardly made a start on either road.

The changes in demographic trends which we have been describing have at least one very interesting aspect in common. They are all trends away from processes of "natural" selection over which man himself has no control, towards processes of selection dictated first by man-made conditions of society and finally by voluntary individual choice. When selection is mainly by deaths, neither society nor the individual has much choice in the matter. When one class of society has only half the birth rate of another class in the same country at the same time because one group uses contraception and the other does not, this is a matter pretty much in the control of society. When the use of contraception is accepted and effective throughout the whole population, choice of size of family is entirely an individual choice, though the choice may be much influenced by conditions created by society. When geographical isolates break down, the individual has a much wider field from which to choose a mate with similar tastes and interests.

At the present time we have no definite indications that any selection for man's higher qualities is actually taking place. We seem to be in a time of change, from a long period of natural selection over which man himself had no control, to a period of selection by individual decisions influenced by the conditions surrounding each individual couple. This new type of selection should be less painful than the old. It might indeed more easily than the old be directed to the improvement of the race.

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MODERN THERAPY AND HEREDITARY DISEASES

By B. M. ASCHNER and R. H. POST

Causal therapy of genetically determined disorders is not feasible, in so far as a genotype cannot be changed. Hence the therapeutical pessimism of many workers in this field. However, by various palliative methods marked success has been achieved in the treatment of several genetically determined anomalies and diseases, as listed in table 1. Nervous and mental diseases have been deliberately omitted from the list.

Welcome though these therapeutical results may be for the patient and physician, for the population geneticist the question arises whether and to what extent the resulting prolongation of life span and the correction of disabilities may lead to increases in the frequencies of the provocative mutant genes in modern populations—genes which formerly were prevented from increasing by natural selection, owing to early death or the curtailing of reproduction of affected individuals.

In order to forecast future increases in gene frequencies the following items about a disorder must be ascertained or estimated: 1. its mode of inheritance and the percentage penetrance of the provocative genes, 2. its incidence in the population, 3. age of onset, 4. net fecundity of affected persons, and 5. their mortality. The last two items may be combined into a single figure.

Table 1. Examples of Hereditary Conditions Amenable to Therapeutic Measures

Therapeutic method	Hereditary conditions responsive to these methods	
Anatomical correction		
a) by orthopedic or plastic surgery	harelip and cleft palate	congenital dislocation of hip
	polydactylism and syndactylism	clubfoot and other deformities
b) by major operations	congenital pyloric stenosis	patent ductus art. *Botalli*
	megacolon	*Fallot*'s tetralogy
Replacement therapy		
a) hormonal	diabetes mellitus	idiopathic (non tbc) *Addison*'s
	athyreosis and hypothyroidism	disease
	primary eunuchoidism	idiopathic tetany
b) other types	pernicious anemia	
Surgical or actinic reduction of over-functioning organs	*Graves*' disease and toxic goiter	pituitary adenoma
	hyperparathyroidism	suprarenal adenoma
	insuloma	pheochromocytoma
Removal of growths producing compression syndromes	goiter	uterine fibroma
Surgical removal of malignant tumors	various malignant tumors	
Correction of vision and hearing	refraction anomalies	glaucoma
	senile cataract	otosclerosis
Prevention or treatment of complications	peptic ulcer	idiopathic thrombopenic
	congenital hemolytic jaundice	purpura (hemophilia)

When the incidence of a hereditary disease is believed to be constant from one generation to the next, the frequency of the provocative genes is said to be in equilibrium, with the total effects of negative selection equal to and balanced by contrary forces which tend to increase the frequency of these genes. For a rare disease there may be only one such force at work—that of mutation. Then the rate of gene increase resulting from a completely effective therapy would be approximately equal to the mutation rate. Higher frequencies must be explained by additional evolutionary forces, such as that of positive selection, which is frequently called "adaptive value".

Perhaps the most logical "a priori" hypothesis in explanation of a high disease incidence is that of selection in favour of the heterozygote.

To illustrate the procedure of forecasting a tentative assay is presented for diabetes mellitus. This disease is chosen because of its high incidence, comparatively simple diagnosis, and particularly because of the quality and quantity of the available literature, even though in this

case the hypothesis of the adaptive superiority of the heterozygote does not appear to be applicable.

Prior to the development of modern therapy diabetes was lethal in most early onsets, and it remained sufficiently deadly throughout a great part of the reproductive period to constitute a relative strong selective force. Assuming that the total effective gene frequency was then constant from one generation to another, we would conclude that its frequency today must be increasing in populations where modern therapy is available.

Assumption of a single recessive autosomal gene is made for simplicity's sake, with no implication that there might not be several genes at several loci. The best estimate of gene frequency seems to be "about .224" after *Steinberg* and *Wilder*. Frequencies of corresponding genotypes are shown on table 2. The actual disease incidence in the U.S. is about 1%.

Table 2

Type of Genes		Approximate Frequency
Normal gene	D	$p = .776$
Mutant allele	d	$q = .224$
Normal genotype	DD	$p^2 = .6$
"Carrier" genotype	Dd	$2pq = .35$
"Diabetic" genotype	dd	$q^2 = .05$
Disease rate (P = penetrance at 20%)		$Pq^2 = .01$

(after *Steinberg* and *Wilder*)

Regarding fecundity, we have found only a few reports which compare the average family sizes of diabetic and pre-diabetic women with those of normal ones. All of them suggest that the average number of pregnancies of diabetic women exceed expectancy.

Six series have been reported which give data for comparing fecundities of the three types of matings which produce diabetic children. These data are represented on table 3. Despite their heterogeneity of origin we have pooled them in order to augment the totals. The average family size of the pooled totals rises steadily from type "a" over "b" to "c". In other words a diabetic and a non-diabetic parent have more children than two non-diabetic parents; and when both parents are affected, the family size is larger still.

These averages are biased since they are derived from families having at least one diabetic child. Smaller families are under-represented in contrast with larger families in all three types of matings because of their

Table 3. Average Number of Offspring in Families Having one Diabetic Child when (a) no Parent is Diabetic, (b) One Parent, and (c) Both Parents are Diabetic

	a			b			c		
Author	No. of families	total children	average size	No. of families	total children	average size	No. of families	total children	average size
Steinberg and *Wilder* [1952]	1589	8253	5.2	370	1990	5.4	22	122	5.6
Von Kries [1953]	1137	4877	4.3	160	663	4.1	8	35	4.4
Harris [1950]	1124	4541	4.0	109	484	4.4	8	43	5.4
Thompson and *Watson* [1952]	828	4664	5.6	166	937	5.6	4	28	7.0
Pincus and *White* [1933]	440	1935	4.4	81	380	4.7	(2 or 3)		
White [1932]	491	1453	3.0	33	101	3.1	2	4	2.0
Totals	5609	25723		919	4555		44	232	
Pooled Averages			4.6			5.0			5.3

smaller chance of including a diabetic child, and also because of the low penetrance of the d gene. Smaller families are under-represented in type "b" matings in contrast with type "c", and even more in type "a" since the progeny of carrier by diabetic matings have a probability of only 50 percent of being dd, while the progeny of carrier matings have a probability of only 25 percent of being dd and thus detected. Therefore, if the fertility of all three types were the same, one would expect the average family size of type "a" to appear greatest, and that of type "b" to apparently exceed that of type "c". Correction of bias would increase the observed differences in average family size rather than diminish them.

Table 4. Average Size of Families Having at Least one Diabetic Child for Three Types of Matings.

Type of mating	Number of matings	Uncorrected for bias	Corrected	
			P = .2	P = .4
Di × Di	44	5.27	4.00	4.42
Di × Ca	919	4.96	3.48	3.77
Ca × Ca	5609	4.59	2.95	3.16
(Fecundity index)		(1.16)	(1.35)	(1.39)

Note: "Fecundity index" is computed from average family sizes as follows: (Di × Ca) minus one half (Ca × Ca); the difference divided by one half (Ca × Ca). It represents the relative superiority of Di over Ca in fecundity.

Table 4 shows the pooled average family sizes of the three types of matings with corrections for bias. The corrections are based on fecundity in the U.S. 1929–1931, excluding sterile marriages, with penetrance taken at two levels, 20% and 40%. Since carriers are of two genotypes—i.e.

100% of the Dd's and 80% of the dd's are carriers—the fecundity indices are further corrected to represent the relative superiority of the dd genotype over the Dd. The fecundity index 1.16 on table 4 when corrected becomes 1.35 taking penetrance at 20%, and 1.39 taking penetrance at 40%.

These indices may be employed as adaptive values for forecasting the increase of the d gene in future generations. It is assumed first that selection favors the homozygote dd over the other two genotypes, Dd and DD. This is justified by the data on table 3 as well as by other evidence. It may cause surprise since the heterozygote is usually considered to have a higher adaptive advantage than either of the homozygotes; but no suggestion of this has been noted in the literature on diabetes, and no "a priori" consideration has been encountered for denying an adaptive advantage to the dd genotype.

The uncorrected index 1.16 which is lower and therefore more conservative than either of the corrections for bias will cause a doubling of the dd's and thus of the incidence of diabetes in about 10 generations (table 5). The corrected indices will cause doubling in six generations with penetrance taken at 20%, and in 5 generations with penetrance taken at 40%. If we assume that selection favors the heterozygotes Dd as well as the homozygotes dd, the rate of increase will be faster still.

Table 5. Changes in Frequency of Gene d (q) and Genotype dd (q^2) for Sufficient Generations to Cause Doubling of q^2 from .05 to .10, with Penetrance at 20% and 40%.

	Uncorrected		Corrected for Bias			
			P = .2		P = .4	
Adaptive value	1.16		1.35		1.39	
Generation	q	q^2	q	q^2	q	q^2
0 (start)	.224	.05	.224	.05	.224	.05
1	.232	.054	.238	.056	.239	.057
2	.240	.058	.253	.064	.255	.065
3	.248	.062	.269	.072	.274	.075
4	.256	.066	.287	.082	.294	.086
5	.265	.070	.306	.094	.316	.100
6	.275	.075	.328	.108		
7	.284	.081				
8	.295	.087				
9	.306	.094				
10	.318	.101				

In these computations no assumption is made as to whether or not the diabetes gene is or was in equilibrium. Only three assumptions are made:

random mating, equal contribution of both parents to fecundity, and that selection favors the homozygote dd. For the last assumption there seems to be tangible evidence. Such an amazingly rapid increase in frequency of the d gene resulting from modern therapy can be attributed only to the more severe, juvenile cases of diabetes.

We wish to emphasize that our interpretation of the apparently higher fecundity of diabetic women is only tentative. Other authors (see *Pyke*) suggest that the fact of having given birth to more children than average will increase the likelihood of dd women to develop the disease. Though we may not yet be quite sure which is the cart and which is the horse between diabetes and parity, it is difficult for us to imagine higher parity causing diabetes in all cases many years after the partus—*Pyke* is dealing exclusively with patients who developed their diabetes after age 45—, also difficult to understand why the larger families of the 19th century did not then induce higher diabetes rates among the mothers. Therefore we tend to believe that higher parity is a result of the d gene and not the cause of higher disease rates.

The high incidence of the disease in all populations presents a particular problem. It is considerably higher than those of most genetically determined diseases. The challenging question arises whether the d gene may have an adaptive advantage, or may have had one in the more remote past; and if so, what was its nature.

Two clues are suggested. One is the well known precocity in general development of many diabetic children. While such precocity is associated with the abnormal and the pathological, it might nevertheless have a survival value, particularly in primitive cultures. If so, the advantage must have been shared by all dd genotypes and not have been confined to those who developed the disease.

Another clue arises from the well known association between diabetes and environmental conditions, particularly food consumption. In ancient and medieval times it was considered a disease of the rich. Modern death rate data frequently show a positive association with higher economic standards.

If this be so, it must mean that penetrance of the dd genotype is lower in the environment of periodic food shortage since the gene frequency cannot be significantly different. The dd genotype is therefore not a liability in such an environment. Carrying this thought one step further, we may assume that the dd genotype may have had adaptive advantage in pre-agricultural environments, i.e. it may have been better adapted to an economy of want than to one of abundance.

If pre-agricultural economies produced lower rates of diabetes and at the same time favored the selection of the d gene, the more recent economies of relative abundance of certain foods with their higher disease rates and consequent selection of diseased individuals must have tended to decrease the d gene's frequency. Hence modern therapy, causing an increase in gene frequency, may be considered to have restored the trend of gradual increase, or at least to have curbed the decline.

If this hypothesis should prove tenable we may represent modern therapy as having restored an environment favorable to the d gene, as were pre-agricultural environments. While, however, the higher frequency of the d gene in a period of apparently low penetrance was comparatively harmless, this is not so under conditions of present day civilization with penetrance higher and the danger of diabetes becoming more and more frequent in the population.

It must be emphasized that our hypothesis of the evolutionary adaptive value of the recessive homozygote and its lower penetrance in pre-agricultural times are unique to diabetes mellitus and do not apply to other genetically determined disorders which are amenable to modern therapy. Unfortunately, there is no other disorder for which sufficient data have been found for the forecasting of future changes in gene frequency. In analogy to our computations on diabetes we may, however, expect a more or less rapid rise in gene frequency.

In *conclusion* we may point out that an ever increasing number of hereditary anomalies and diseases are becoming amenable to modern therapeutic methods with, in certain cases, an ensuing rise in frequency of the mutant genes. According to our tentative estimate for diabetes mellitus a doubling of the frequency of the dd genotype may be reached in five to ten generations, based upon the trend of the preceding generation. With the progress of knowledge and the accumulation of statistical data on genetically determined diseases, forecasts of gene frequency changes promise to become increasingly satisfactory in the near future.

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THE INFLUENCE OF INCREASED EXPECTATION OF LIFE ON THE GENETIC IDENTITY OF HUMAN POPULATIONS

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At the present time there are fairly sharp differences of opinion about the possibility that interference with natural selection is influencing the genetic constitution of human populations. Some people believe that genetic equilibrium is being seriously disturbed, and that unless appropriate eugenic measures are taken the results are likely to be serious. Others consider that such fears are exaggerated, and that in any case the measures suggested are for one reason or another likely to prove to be unacceptable or ineffective. Although these differences in viewpoint are perhaps not wholly of scientific origin, the fact that experienced observers arrive at quite different conclusions when confronted with the same

evidence reflects both the extreme complexity of the problem and the inconclusive nature of much of the evidence.

The grounds upon which it has been concluded that genetic deterioration has occurred or is likely to occur in man are well known. First, it has been observed that measured intelligence is negatively correlated with sibship size, and it has been assumed that this is a recent phenomenon attributable to the practice of contraception, rather than a long-standing one resulting from biological variation in fertility. Second, it has been estimated that human disease attributable to mutation is common (*Muller* [1950]), and it is suggested that an increase in its incidence is a probable consequence of improved expectation of life. Let us note that the first of these two lines of evidence turns upon the trend of the birth rate, and the second upon the trend of the death rate.

Of various objections that have been raised to these views there are two which I wish to examine. The first is that a decline of intelligence cannot be inferred from the negative correlation between intelligence and sibship size, because differential fertility of biological origin maintains genetic stability. The second objection is that even if it is true that the frequency of certain mutant genes has increased, in the changed environmental circumstances which have permitted the increase, the genes cannot be regarded as undesirable.

1. The character most frequently discussed in relation to differential fertility of biological origin is intelligence. It is well known that individuals of very low intelligence are—for reasons other than conscious limitation of family size—relatively infertile, but it is by no means certain that the same is true of individuals of high intelligence. If it has any significance in this context the association between success and fertility of Harvard graduates (*Phillips* [1927]) is against it, and I have a vivid personal recollection of the interruption of a social occasion in the United States by the arrival of what I took to be a girls' hockey team, whose members were subsequently identified as the female offspring of our eugenically superior host. Many such instances could be assembled to offset the examples of infertility among medieval scholars and men of genius, and it seems very doubtful whether we shall be able to reach a satisfactory conclusion about the natural fertility of very intelligent people, who must have been among the first to recognize the advantages of childlessness or small families, and the most efficient in the use of whatever contraceptive measures were available.

Another character which has been considered in relation to differential fertility is birth weight (*Penrose* [1955], *Fraccaro* [1956]), for which a

substantial body of reasonably accurate data is on record. Apart from this advantage it seems a particularly unsuitable example upon which to explore the influence of selection. In the first place in man, as in several other mammals, the variance of birth weight is determined mainly by the uterine environment. The weight of a child at birth is more closely correlated with the height of the mother than with the height of the father (*Cawley*, *McKeown* and *Record* [1954]). A striking demonstration of the same effect was obtained by reciprocal Shire-Shetland crosses (*Walton* and *Hammond* [1938]) in which the birth weight of the hybrid foal with a Shetland dam was a great as that of the foal of pure Shire parents. Secondly the influence of foetal genotype is evidently not constant over the whole range of weight, being greater when birth weight is high than when it is low. Indeed it is quite possible that foetal genotype has no influence upon the weight at birth of most foetuses delivered at low weights at which mortality is highest. In multiple pregnancy, for example, the low birth weight is attributable almost entirely to retardation of foetal growth in late gestation (*McKeown* and *Record* [1952]), the retardation being apparently due in part to influences within the uterus, and in part to influences outside it (*Eckstein* and *McKeown* [1955]). In placenta praevia, on the other hand, low birth weight is due mainly to early onset of labour (*Record* and *McKeown* [1956]). Although the mechanism which leads to low birth weight is different in these two examples, in both it is apparently independent of foetal genotype.

A third character upon which the influence of selection has been examined is stature, and it has been suggested that because stature, like intelligence, is negatively correlated with family size, the fact that it has not declined is significant (*Penrose* [1950]). One would prefer to say that if stature has not increased it would be significant. There are sharp differences in mean height (2.5 inches between Scottish males in Classes 1 and 5) in relation to social class (*Clements* and *Pickett* [1952]), and the improvement in standard of living during this century would certainly have been expected to lead to an increase in stature. *Clements* [1953] concluded that there is no clear evidence that mean height of men has altered in Great Britain during the past hundred years, but the observations on adult height in the 19th century possibly do not justify a firm opinion. Using measurements on outpatients in a Swedish hospital, *Holmgren* [1952] showed that stature of male adults increased by about 3 cm between 1914 and 1930. No conclusion can be based on the increased height of school children, which may reflect a change in the age at which maximum height is reached, rather than a change in maximum height (*Clements* [1953]).

But although the evidence in respect of characters such as intelligence, birth weight and stature does not provide very strong support, there is no reason to doubt that in freely breeding populations differential fertility of biological origin plays an important part in maintaining genetic stability. It is equally clear that this mechanism can be disturbed by selective restrictions on breeding, whether the restrictions are imposed compulsorily, as in the case of farmyard animals, or voluntarily, as in the case of man. From the time that it became relatively easy for human populations to separate the act of copulation from its effects, the possibility that the mechanism of selection has been disturbed has certainly existed. It seems unreasonable to reject this possibility in respect of characters such as intelligence or stature, on the grounds either that they are influenced by the environment, or that we cannot predict the results of selection without knowledge of their genetic basis and of the breeding systems. Extreme variation of weight and length has been produced by stock breeders with knowledge only of the phenotype.

2. The second possibility which I wish to consider is that if modification of the mechanism of selection has resulted in increased frequency of certain genes, in the changed environmental circumstances which have permitted the increase the change is of little consequence. *Snyder* and *David* [1953] have drawn attention to the error which results from applying the world "deleterious" to mutant genes rather than to their effects, and obviously it would be incorrect to describe as harmful a gene whose frequency had increased in a wild animal population as a result of a change in the environment. In man the problem is more complex. If the increase in gene frequency is a secondary consequence of a more or less permanent change in the character of the environment—for example of a shift from rural to urban life—no ill-effects need be anticipated so long as the change is maintained. The fact that the population of Western Europe is almost certainly more susceptible to cholera today than it was a hundred years ago probably does not matter, because the source of infection is effectively controlled. The circumstances are quite different if increased gene frequency is a direct result of medical therapy. In the first place a disease which is compatible with survival and reproduction may have unpleasant features for those who are afflicted. And secondly, the services required to maintain the population of affected individuals are provided immediately at the expense of alternative uses of medical effort, and ultimately at the price of retardation of advance in the general standard of living. An increase in the frequency of diseases—even those

which can be controlled as effectively as diabetes and pernicious anaemia —could not be said to be of no consequence.

I have suggested that if the negative correlation between sibship size and intelligence does not permit us to conclude that intelligence is declining, the fact that biological variation in fertility contributes to genetic stability also does not exclude the possibility that birth control has been practised most frequently and most efficiently by intelligent people. And if the incidence of diseases of genetic origin has increased as a result of a decline of the death rate, to the extent that this increase has resulted from medical therapy it has drawn on limited resources and must be regarded as undesirable. For these reasons I do not believe that we can dismiss the possibility that there has been a change in the genetic structure of human populations, or accept the view that such a change would necessarily be unimportant. Both suggestions appear to result from pressing the analogy with animal populations without sufficient regard for the unique set of circumstances which have existed since the population of Western Europe began to rise in the late 18th century. These circumstances were unique in two respects. In the first place, the introduction of effective measures of birth control made it possible to superimpose upon the pattern of natural fertility a new pattern not primarily determined by the activity of the ovary and testis. It is at least possible that this change had some genetic significance, and more than likely that it had social significance. (For even if no genetic influence were involved we could scarcely regard it as unimportant if family limitation were practised most intensively by those who could create the most favourable environment for their children. This point was discussed by *Hogben* [1931] in relation to mental defect.) Secondly, although the reduction of the death rate was attributable in part to environmental changes which could be regarded as comparable to those which influence the survival of wild animal populations, to the extent that it was due to medical therapy it can fairly be described as unique.

Let us now consider the two questions: Is it likely that contraceptive practice has influenced the trend of intelligence? And has the decline of mortality resulted in an increase in the incidence of diseases of genetic origin? I hope I may be excused for referring mainly to the data for England and Wales, with which I am most familiar, and for presenting briefly and without support those observations about which I believe there is no serious dispute.

The influence of contraception

For anyone interested in human genetics, the evidence concerning intelligence and fertility is what Hamlet is to the actor, or Madam Butterfly to the soprano, a challenge which sooner or later he must meet however limited his equipment and however regrettable the consequences. If excuse is needed for referring to it again, it must be that a correct interpretation may depend less upon new evidence than upon the way in which we look at the observations which are already available.

Although the birth rate in England and Wales undoubtedly fluctuated in earlier centuries as a result of changes in mortality, and possibly also, though less certainly, in relation to other influences such as variation in age at marriage (*Habbakuk* [1953]), it was not until the late 19th century that it began to show the effect of international restriction of family size. *Kuczynski* [1938] found little evidence of the practice of birth control in the English demographic literature of the 17th century: it is doubtful whether abstinence has ever had much influence on population trends (except possibly in Eire, where the coincidence of a relatively late mean age at marriage and low illegitimacy rates with the alleged infrequent use of contraceptives remains one of the unsolved demographic mysteries); and abortion can have been neither common nor safe.

Nevertheless it is quite probable that the pattern of differential fertility before the 19th century was not wholly determined by biological causes. Some fertile people, including some very intelligent people, may have practised coitus interruptus, and a few no doubt regarded celibacy as a small price to pay in order to remain childless. Recognition of this fact is of some importance, since it will be suggested that the view that contraceptive practice may have altered the pattern of differential fertility in the 19th century does not rest on the belief that formerly all variation is fertility, particularly in relation to intelligence, was necessarily biological in origin.

What can scarcely be doubted is that the use of effective contraceptive measures since the late 19th century, on a scale which was rapidly reflected in the birth rate, may have altered the pattern of differential fertility in relation to intelligence. Whether in fact it has done so cannot be inferred from the available evidence, for as *Penrose* [1950] and others have noted, the negative correlation between sibship size and intelligence might be attributable to biological causes. There are, however, two points about the evidence which should be mentioned. The first has already been referred to, and is that recognition of biological variation of

fertility in relation to intelligence, and of the possiblility that some intelligent people have always excercised a degree of control of the size of their families, does not exclude a further differentiation since the 19th century as a result of contraception. The second point is that no conclusion about the recent trend of intelligence can be based upon the observation that a variable such as stature, which is also negatively correlated with sibship size, has not decreased. For the only question which arises in the present context is whether family size has been more restricted by the intelligent than by the less intelligent. If contraceptive practice is associated with other variables such as stature, it can only be as a secondary consequence of their correlation with intelligence.

My own view is that the available evidence does not permit us to say with confidence that intelligence has declined or has not declined, and that the most that we can attempt is to give a common sense answer. And common sense seems to me to suggest that it is very likely that intelligent people made earlier and more efficient use of contraceptive techniques, as they must have made earlier and more efficient use of the other amenities provided by the 19th century sanitary revolution. We must now enquire whether this conclusion has any serious or enduring significance.

At once we are confronted with the question of the extent to which intelligence, in the sense in which we are using the word, is affected by environmental influences. For reasons explored fully by *Hogben* [1951] in his examination of the formal logic of nature and nurture, the question cannot meaningfully be expressed in so simple a form. The low test score of a child in Central Africa may be wholly attributable to his environment, whereas that of a child in a well-to-do family in Western Europe may be almost wholly attributable to his inheritance. It is obvious, however, (a) that the more uniform the environment to which individuals have been exposed, the greater the genetic significance which can be attached to their test performance, and (b) that results of intelligence tests hither— to have reflected in a considerable and variable degree differences in educational opportunity.

Present evidence gives no clear answer to the somewhat unrealistic question whether, in a uniform environment in which contraceptives were readily available, variation in fertility in relation to intelligence would be greater than could be attributed to biological influences alone. But it seems reasonable to suppose that it would, since the level of intelligence below which people are incapable of practising contraception is probably higher than the level below which they are invariably infertile. So far as I am aware there is no proof of this, but I imagine that no one would doubt

that there are fertile individuals of low innate intelligence who are incapable of limiting the size of their families. (Let us note that the significance of this statement is not cancelled by recognition that there are also fertile individuals of high intelligence who choose not to limit the size of their families.) Their incidence is unknown, but is probably low, and the effect of their reproduction on the pattern of differential fertility would be determined to some extent by the practice of other fertile people. In a society in which small families have considerable advantages, those with the wit to limit family size will do so, and the influence of the larger families of fertile individuals of low intelligence would be greater than in a society in which the penalties for having large families were less severe.

For these reasons I believe that the spread of contraceptive knowledge has probably had some influence on the trend of the intelligence which is measured by tests, and a smaller and perhaps trivial influence on the trend of the genetic component in intelligence. This conclusion is based, not on the negative correlation between measured intelligence and sibship size, which might be largely due to biological variation, but on consideration of the probable extent to which contraception has been practised by individuals of varying intelligence.

We must finally consider whether if such a trend continues it is of any practical importance. It seems to be widely believed that a general increase in intelligence would be highly desirable, and that even a small decline, particularly of the genetic component in intelligence, would be a serious matter which would require urgent action. This opinion overlooks the fact that there exists an immense reserve of unused ability which is more accurately assessed in *Gray*'s "Elegy in a Country Churchyard" (a poetic expression of the nature nurture viewpoint) than in some discussions of the trend of intelligence. Unless we are prepared to believe that there have been some remarkable mutations at different times in history—in 15th century Florence, in Elizabethan England and in the English Midlands at the birth of the industrial revolution, to take three notable examples—we must conclude that it is only in certain places and for very short periods that any considerable part of the capacity available has been exploited.

Moreover, it is by no means certain that we would know how to use a larger number of intelligent people if they became available, or that we should be able to reward them if they could be employed. A large part of the world's work needs little intelligence, and of a considerable part of the remainder it might be said, as Mr. *Raymond Chandler* has said somewhere of the Los Angeles police force, that it requires good men, but has

little in it to attract good men. It is true perhaps that there are few jobs which could not be done better by intelligent than by less intelligent people, but if job placement ever becomes a serious international problem, my own guess is that it is more likely to be because many occupations demand ability but do not reward it, than because the general level of intelligence is inadequate.

The Influence of Increased Expectation of Life

We must now enquire whether the decline of mortality may have resulted in a increased incidence of genetic disease, and if so, whether the reasons for the decline are such that the increase would be undesirable.

Until the late 18th century mortality in England and Wales was so high that in spite of a high birth rate the population increased only very slowly. According to *Edmonds* [1835] more than half of the infants baptized in London in the period 1770–89 were dead before the age of 5, and *Brownlee* [1925] estimated mortality in 18th century London during the first two years of life to be 300–400 per 1000 live births. The high mortality was chiefly attributable to infectious disease, which must have had a significant influence on human evolution, as suggested by *Haldane* [1949].

Although deaths were not registered before 1837 it is generally believed that the death rate began to decline during the last third of the 18th century at about the time when the modern rise of population began. The traditional view (*Griffith* [1926]) has attributed the fall to advances in medicine. This opinion was questioned by *Habakkuk* [1953], who suggested that it was probably secondary to a rising birth rate which resulted from a reduction in age at marriage brought about by economic developments of the period. *McKeown* and *Brown* [1955] examined the medical measures introduced during the 18th century, and concluded that they could have had no appreciable effect on the national death rate. Nevertheless they thought it unlikely that the decline of mortality was secondary to a rising birth rate, and suggested that it resulted from a reduction of mortality from infectious disease. Since this view has some bearing on the possibility of genetic change, the reasons for it will be stated briefly.

In assessment of the relative significance of birth rate and death rate in the late 18th century three observations are of first rate importance: mortality was very high: the high death rates were chiefly due to infectious disease; and the highest risks were experienced by infants and

young children. The level of the birth rate is less important in this context, although in general it was undoubtedly high. Under these conditions a decline of mortality would result in an increase of population and probably also of the birth rate; a rise of the birth rate would have relatively much less effect on population and would be followed by an increase in mortality (because the additional children would be added chiefly to existing families, and mortality increases sharply with increasing family size). A decline of mortality is therefore the more plausible explanation of the rise of population, and the most acceptable reason for it is a reduction in the incidence of death from infectious disease. If we accept the view that this reduction was not due to medical effort, unless we are prepared to attribute it wholly to a change in the character of the infectious diseases we must conclude that it resulted from improvement in economic and social conditions.

In the first three-quarters of the 19th century both the death rate and birth rate remained relatively constant and the continued rise of population was attributed mainly to the fact that by 1800 the death rate was considerably below the birth rate. Since about 1875 both rates have fallen, and although the decline of the birth rate has been even more rapid than that of the death rate, the population has continued to increase. We must now consider the reasons for the decline of mortality during the past 75 years.

National statistics leave no doubt that the improvement has been mainly due to a further marked reduction in mortality from infectious diseases; there has been relatively little change in mortality from non-infectious causes. This is reflected in life expectation at different ages: the really marked increase has been in the youngest age groups, and there has been little improvement in life expectation of adults. The probable explanation of the anomaly (to which *Muller* [1950] has referred) that length of life has traditionally been regarded as three score years and ten, is that it was assessed only for individuals who survived the hazards of infancy and childhood. Until the 19th century the period between birth and maturity must have been thought of in much the same way as we now think of the period between conception and birth, an interval for which reliable statistics are not available and in which mortality is in any case so high that if deaths were included they would make nonsense of the calculations.

The reasons for the decline of mortality since 1875 are not the same for every infectious disease. The control of cholera and typhoid is due to hygienic measures; the elimination of smallpox is largely—although by no means entirely—the result of vaccination; the decline in mortality from

tuberculosis is mainly attributable to a general advance in living conditions (the effect of therapy is detectable only during the last decade); and the marked change in the character of scarlet fever, measles and influenza appears to owe nothing to therapy or environmental change, but to be the result of a shift in the balance between the virulence of the infective organism and the immunity of the host. Nevertheless two generalizations appear to be justified. They are (a) that specific preventive and curative therapy have had little effect on the decline of mortality from infectious disease (smallpox and diphtheria are the only notable exceptions and their contribution to the total mortality in the late 19th century was not large), and (b) that the most important external influence has been an improvement in the environment. This influence has been superimposed upon the "normal" fluctuations of virulence and resistance which reflect the interaction of nature and nurture on both the infective organism and its host.

It is against this background that we must attempt to come to a decision about the relation between the decline of mortality and selection. The problem arises predominantly in respect of the infectious diseases, and our conclusions are suggested by the reasons for their decline.

(a) In the case of diseases such as influenza, scarlet fever and measles, in which the reduction of mortality is attributable to a shift in the balance between immunity and infection, it cannot be said that there has been any relaxation of selection. For although the course of these infections has unquestionably been influenced by genetic selection it has been essentially independent of medical and other intervention.

(b) In the case of infectious diseases whose decline has been due mainly to improvements in the environment, there must have been an increase in the proportion of susceptible individuals. The example of cholera has already been mentioned. Whether this increase has any serious significance depends upon the effectiveness and character of the measures used to achieve control. Broadly it is probably true to say that if exposure to infection can be prevented, and if the cost of the requisite environmental measures is not excessive, the increase in the proportion of susceptible persons is of little consequence. In the case of most of the infections to which we are referring under (b) both conditions are met. Indeed many of the environmental changes which have had a profound influence on mortality from infectious disease were not introduced primarily as health measures. They were part of a general improvement in the standard of living which began before the nature of the infectious diseases was understood, and would be maintained even if there were no

specific health grounds for their retention. Under such conditions an increase in the incidence of susceptible individuals can scarcely be attributed to relaxation of selection, but may be regarded as comparable to the modification which occurs in the genetic constitution of wild animal populations in responce to a natural change in the environment.

(c) The circumstances are different in the case of infectious diseases whose control relies upon specific therapy. But as stated earlier their incidence is low, and the successful measures are of so simple a kind that their cost is of little consequence. We cannot, of course, predict the long term effects of immunization procedures on the epidemiology of infectious disease, although there is as yet no evidence that they are undesirable.

We should not end this discussion of the infectious diseases without referring to the possibility that the decline of mortality from infection may have resulted in increased frequency of some genetically determined conditions. In mongolism, for example, infection is a common cause of early death, and it is probable that mongols now live longer than they once did. Although in this case the increased expectation of life has had no effect on reproduction, the possibility that the incidence of genetic disease has increased slightly as a consequence of lowered mortality from infection cannot be entirely excluded.

Finally, we must consider the possibility that as a result of medical intervention there has been relaxation of selection in respect of diseases other than infections. There is little doubt that as a rule the effectiveness of specific medical measures is grossly overestimated. This is not the occasion to attempt a detailed evaluation of medical achievement, but two conclusions must be mentioned. The first is that the influence of specific preventive or curative therapy was trivial before the beginning of the present century; vaccination against smallpox was the only important measure. And second, even today the number of conditions other than infections of which it can be said confidently that treatment profoundly alters their course is still very small. But in respect of these few diseases—diabetes is a good example—it seems probable, though not certain, that if they are manifested early in life incidence has increased. (The reservation is necessary because with some conditions affected individuals might live longer but remain infertile.) If this increase has been brought about at the expense of medical resources, or if the disease has unpleasant features for those affected, it seems inevitable that we should regard the trend as undesirable. The main source of comfort is not that relaxation of selection would not matter, but that so far it has hardly occurred.

To sum up. It has been suggested that the main cause of the decline

of mortality in England and Wales since the late 18th century has been a reduction of the incidence of infectious disease. In part this reduction has resulted from a shift in the balance between immunity and infection, but mainly it has been brought about by improvements in the environment. The contribution of specific preventive or curative therapy is considered to have been small. It seems very likely that the proportion of susceptible individuals has increased as a result of selection. To the extent that this increase has been brought about by a "natural" change in the character of infectious diseases it obviously cannot be attributed to medical or other intervention: and to the extent that it has resulted from changes in the environment, because these changes are mainly of a permanent kind the increased susceptibility is probably of little significance. In the case of diseases other than infections it is emphasized that the influence of treatment on prognosis is still very limited. But in the few diseases in which there may well have been an increase in incidence it is suggested that if treatment uses medical resources, or if they have unpleasant features for those affected, the increase in incidence cannot be regarded as unimportant.

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SOURCES OF VARIATION IN THE HUMAN SEX RATIO AT BIRTH

By T. McKEOWN

Interpretation of variation in the sex ratio of human births is complicated by uncertainty about the extent to which it reflects (a) variation in the sex ratio at conception and (b) the influence of prenatal losses. Because the ratio (percentage of males) is above 50 in livebirths, stillbirths and the late abortions which are available for inspection, it has been thought that it is probably above 50 at conception. And if this view is accepted it is perhaps natural to suppose that changes in the sex ratio at birth in association with variables such as maternal age may reflect similar changes at conception.

These views were questioned by *McKeown* and *Lowe* [1951], chiefly on the grounds of uncertainty about the sex ratio of early abortions whose incidence is undoubtedly high. In most series the proportion of abortions reported in the early months has been low, either because sex was not readily identified, or because the aborted material was not available for examination. Reasons were suggested for doubting whether the sex ratio of late abortions and stillbirths were acceptable as a guide to ratio of abortions in the early months: (a) different causes of abortions have different sex ratios; (b) the composition of abortions by cause changes throughout pregnancy; and (c) not all causes of abortion (for example, anencephalus and spina bifida) have the same sex ratio at different stages of gestation. In these circumstances it was suggested that an estimate of the sex ratio at conception was not warranted without much fuller information about early abortions than is yet available. And it seemed possible that the decline in the sex ratio of total births (livebirths and stillbirths) with a variable such as maternal age, might be attributable to an increase in the sex ratio of abortions, in the same way that the difference between total births and livebirths is explained by the trend of the sex ratio of stillbirths (*Lowe* and *McKeown* [1950]).

Data which may have some bearing on interpretation of variation in the sex ratio have become available through examination of sex differences in length of gestation in mammals (*McKeown* and *MacMahon* [1956]). This enquiry was undertaken because it was noted (a) that in the guinea pig and in man there was a fairly marked decline in sex ratio of offspring with increasing length of gestation, and (b) that the association between sex and gestation was not the same in all species. In the cow, for example, sex ratio of calves increases as the period of gestation increases. It was found, as might have been expected, that these changes in sex ratio were reflected in variation in the distribution of the two sexes according to length of gestation.

Further investigation suggested that in man the earlier delivery of male foetuses might be attributable to their greater weight, for first born males and second born females—which differed only slightly in weight—mean duration of gestation was approximately the same. The same explanation could not, however, be accepted for the cow, since the lighter female calves are delivered earlier, and there is in any case little evidence that weight has much influence on the time of onset of parturition (for example, litter size has little effect on the period of gestation.) Unless we are prepared to believe that there is a sex difference, attributable to something other than weight, in the period between fertilization and birth, it

seems probable that in the cow gestation is longer for males than for females because the proportion of males conceived is high if mating takes place early in heat.

Evidently the same explanation cannot be offered for the sex difference in length of gestation in man. But in man gestation is dated from onset of menstruation, which is of course unrelated to sex of offspring. The fact that when so dated gestation appears to be longer for females than for males does not exclude the possibility that in man, as in the cow, a raised proportion of males results from matings early in the cycle.

This last suggestion has no more support than the observation that it seems to be the most acceptable explanation in the cow, and it may be questioned whether it is profitable to carry speculation much further. But it seems worth noting that if sex of offspring is influenced by time of mating, it would provide an explanation for some of the anomalies in the behaviour of the human sex ratio. For it is probable that an increase in the frequency of matings would tend to increase the proportion of early fertilizations and to raise the sex ratio. This might explain the rise in the sex ratio associated with wars (when increased frequency of intercourse in restricted periods is a probable consequence of separation of husband and wife) and its decline with maternal age. It might also account for an independent association between sex ratio and father's age, which has been suggested, but not firmly established.

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SUR LA MÉTHODOLOGIE DE L'ISOLAT

Par J. SUTTER et L. TABAH

On doit la notion d'isolat au Suédois *S. Wahlund* [1928]. Au cours de ses recherches sur la composition génétique d'une population et les corrélations existant entre différents caractères, il envisagea le cas où deux populations voisines, également panmictiques et de mêmes caractéristiques démographiques, échangeraient une partie de leurs individus. Une grande population humaine n'est formée que de populations partielles, limitées dans leur extension propre par des facteurs de divers ordres: géographiques, sociaux, religieux, professionnels, etc. C'est à chacune de ces populations partielles que *Wahlund* a donné le nom d'isolat. L'isolat peut encore être représenté correctement par la population à l'intérieur de laquelle chaque individu a la possibilité de trouver son conjoint. Cette notion de population partielle s'est révélée être aussi importante en biologie végétale et animale qu'en biologie humaine.

Dès l'année suivante, *Dahlberg* [1929] a proposé d'estimer, dans le cadre de la panmixie, la dimension de l'isolat, autrement dit le nombre d'habitants qu'il comporte, à l'aide du nombre des mariages consanguins du 4^{e} degré (cousins germains) qui s'y pratiquent. A cette occasion, *Dahlberg* a introduit une notion démographique importante en soulignant que le nombre des mariages entre cousins dépendait étroitement, à la fois de la dimension de la population et de la dimension des familles. Il a donné la formule que nous rappellons parce qu'elle a été, depuis, utilisée fréquemment. Appelons b le nombre moyen d'enfants qui, au sein de chaque fratrie, arrivent à l'âge adulte et se marient, et a le nombre d'individus de cette catégorie dans la population toute entière. Si l'on choisit un individu au hasard dans la population, il aura en moyenne b (b — 1) cousins germains. Mais le total des individus de cette catégorie

avec lesquels il peut se marier est $\frac{n}{2}$; la probabilité c pour un mariage avec son cousin germain ou sa cousine germaine est alors $c = \frac{2\,b\,(b-1)}{n}$ et $n = \frac{2\,b\,(b-1)}{c}$. On a publié par la suite des formules donnant la dimension de l'isolat à partir des mariages entre parents du 3e degré et entre cousins des 5e et 6e degrés. A partir de ces données, il est aisé, toujours dans le cadre de la panmixie, d'établir des modèles et de rechercher comment évolue la composition génique d'une génération à l'autre, sous l'influence de facteurs comme les migrations ou les variations observées au niveau de la dimension moyenne des familles.

Pour importante que soit cette acquisition du point de vue méthodologique, on doit reconnaître que la panmixie où l'on suppose, en gros, que la population est fermée, que les mariages s'y font au hasard et que la fécondité y est identique pour tous les couples, s'écarte trop des faits réels. On peut rassembler en six points l'ensemble des faits d'observation qui s'y opposent:

1. L'effectif et les limites de la population: le nombre des individus qu'elle comporte et leur localisation géographique.
2. Les migrations.
3. La consanguinité: il existe dans la population des mariages consanguins dûs à l'intérêt ou aux structures de parentés particulières à certaines cultures.
4. Les mutations: un gène ou plusieurs, aquièrent subitement une nouvelle qualité d'expression qui est transmissible.
5. La sélection: il existe une fécondité différentielle.
6. Le choix du conjoint positif ou négatif: les individus porteurs d'un même caractère se marient plus volontiers, ou non, entre eux que ne le voudrait le hasard.

Ces six points nous permettent d'apprécier comment la méthodologie de l'isolat doit, dans la pratique, s'adapter aux circonstances qui différencient les populations les unes des autres.

Il y aurait beaucoup à dire dans ce sens sur la méthodologie de l'isolat, mais nous devons nous limiter. Ainsi, dans tous les pays qui disposent d'un état civil, on doit tenir compte des séparations administratives pour estimer à la fois la dimension des isolats et l'évolution de l'endogamie mesurée par le nombre des mariages consanguins. L'examen des 600 communes de deux départements français, sur plusieurs périodes depuis 1870, nous a montré que le fait de la consanguinité présentait une forte hétérogénéité. Dans le département du Finistère par exemple, au cours de

la période 1919–1929 des communes comme Crozon (9 000 h.) et Plouhinec (9 000 h.) ont eu respectivement un taux annuel moyen de 13 et 18% de mariages consanguins (jusqu'au 6e degré inclus), alors que des communes voisines présentaient des taux bien moindres. La nécessité de plier la méthodologie au partage administratif découle encore du fait que l'évolution de la consanguinité, au sens même de l'éclatement des isolats, n'a pas suivi le même rythme au cours du temps, si l'on envisage les communes en les groupant suivant le nombre de leurs habitants. On voit, par exemple, que la diminution de la consanguinité a été plus rapide de 1870 à 1954 dans les communes les plus peuplées, mais que ce phénomène n'a rien de systématique car les communes de 1 000 à 1 100 habitants, dans le Finistère par exemple, ont évolué beaucoup plus lentement sur ce plan que les communes de 2 000 à 2 500 ou de 700 à 800 habitants. Au fond, on se heurte ici à des problèmes de structure sociale et à des phénomènes culturels qu'il est bon d'avoir toujours à l'esprit quand on étudie ces problèmes.

Il est évident que dans l'étude des isolats, on sera de plus en plus amenés à tenir compte des différences culturelles existant entre les populations. Ces structures imposées par les divers modes des institutions, varient d'une culture à l'autre, contrôlent les structures mêmes des isolats et imposent des adaptations méthodologiques. Depuis quelques années, l'éthnologie nous a appris combien les structures de la parenté étaient diverses et combien elles pouvaient varier de tribu à tribu ou de groupe à groupe. Les mariages préférentiels inhérents à certains peuples comme la règle qui semble assez générale (*Lévi-Strauss*) du mariage matrilatéral, autrement dit du mariage préférentiel avec la fille du frère de la mère opposé au mariage avec la fille de la sœur du père, semble en elle seule devoir perturber déjà la méthodologie classique.

Les tabous atteignant certains mariages consanguins agissent dans le même sens. Au cours de ce congrès, nous avons montré le fait pour l'isolat des eskimos polaires où le tabou existant pour les mariages entre cousins jusqu'au 6e degré fait disparaître pratiquement toute possibilité de mesure de l'endogamie par ce phénomène. Même dans les populations de type occidental, on peut voir des phénomènes du même ordre. Ainsi, dans l'Ile de Sein (Finistère), où les mariages consanguins sont fréquents, nous avons observé l'absence totale de mariages entre cousins germains au cours de la période 1919–1930, pour un pourcentage de 23 intéressant les mariages du 6e degré. Les pêcheurs de cette île estiment anormal que les frères et sœurs favorisent le mariage de leurs enfants respectifs. On doit donc considérer que la méthodologie classique de l'isolat est inappli-

cable à tous ces cas et qu'il est nécessaire de l'assouplir, pour pouvoir utiliser sa signification, à toutes les innombrables circonstances qui peuvent se présenter dans le cadre de la structure de la parenté, phénomène culturel polymorphe.

Si l'on s'en tient à l'effectif des isolats et à leur limite, le phénomène le plus important qu'on a pu observer dans la période moderne est leur éclatement. On a vu disparaître rapidement, dans les populations de type occidental, les mariages consanguins, a mesure que la dimension des isolats s'accroissait et qu'un grand nombre de populations partielles fusionnaient. Nous avons publié des chiffres détaillés intéressant deux départements français, dont un depuis 1812. Ce phénomène qui semble généralisé témoigne que, d'une génération à l'autre, la dimension des isolats s'est, récemment, régulièrement accrue.

Ce phénomène et sa mesure reposent le problème méthodologique fondamental. Si l'on admet en effet que le nombre des mariages entre cousins germains par exemple, est un test fidèle de la dimension de l'isolat, il est évident que sa diminution va de pair avec l'augmentation de l'effectif caractérisant la population partielle. Mais des doutes ont été souvent exprimés visant la valeur de ce test : nous-mêmes en 1950. *Morton* en 1955; ce dernier auteur s'est efforcé de montrer que les mariages consanguins des différents degrés de parenté, ne pouvaient en aucune façon assurer la mesure de la dimension de l'isolat puisque cette dimension pouvait varier du simple au décuple, suivant qu'on s'adressait aux mariages entre oncles et nièces ou entre cousins issus de germains par exemple.

On peut répliquer à cela qu'il est illogique de comparer, sur le plan de l'estimation, la signification d'un mariage entre oncle et nièce et celui entre cousins germains ou issus de germains. Pour notre part, nous avons montré que les deux premières catégories étaient critiquables pour l'estimation, alors que ceux du 6e D., cousins issus de germains, avaient sur le plan démographique réellement observé, une bien plus grande signification dans une optique panmictique. Ils se rapprochent tout au moins davantage de l'hypothèse que les mariages d'un autre degré.

Le problème de la validité du test des mariages consanguins, met en jeu, pour être résolu, deux conceptions et deux écoles: celle de *Sewall Wright* et celle de *Dahlberg*. On a opposé récemment (*Morton* [1955]) les «isolats» de *Dahlberg* aux «neighbourhoods» de *Wright*, autrement dit, la notion d'isolat mesurée par la consanguinité à la notion de ce qu'on appelle en français la «consanguinité de position».

Dans l'optique de *Wright*, qui s'applique à des problèmes d'élevage

d'animaux, on préconise de calculer la dimension de l'isolat et son évolution à partir de l'étude de la variance des distances séparant les lieux de naissance des parents et des enfants. Si cette opération est facile pour les bovidés où les généalogies sont régulièrement publiées et où chaque taureau, grâce à l'insémination artificielle, est capable de féconder un grand nombre de vaches et de transmettre ses gènes à de longues distances, il n'en est pas de même dans l'espèce humaine.

Pour obtenir chez l'homme des statistiques qui doivent nécessairement porter sur des dizaines de milliers d'individus et intéresser les lieux de naissance d'une génération à l'autre, on se heurte à des difficultés insurmontables. Dans la plupart des pays, les documents administratifs, tels que actes de mariage ou carnets de famille, ne permettent pas, en effet, de connaître simultanément le lieu de naissance des enfants et ceux des parents. Il est beaucoup plus facile de connaître les domiciles respectifs des parents et ceux des jeunes époux au moment du mariage. Si l'on se borne à rechercher l'évolution de la distance séparant les domiciles des époux au cours du temps, on recueille des données intéressantes sur l'éclatement de l'isolat puisque cette distance s'est manifestement allongée au cours du siècle dernier, dans les pays d'Occident, et qu'elle a été de pair avec la disparition des mariages consanguins.

On ne sait pas encore si les deux génétiques peuvent être logiquement opposées. Pour notre part, nous nous sommes proposés de rechercher si le test des mariages consanguins peut être en quelque mesure relié à l'évolution de la distance séparant les domiciles des époux. Pour démontrer le fait, nous avons étudié simultanément, dans les 600 communes des 2 départements français observé, si la disparition des mariages consanguins allaient bien de pair avec l'augmentation de la distance des domiciles des époux. L'étude étant en cours, nous ne pouvons donner d'indications définitives. On peut cependant affirmer que l'impression est que le test de la consanguinité ne paraît pas être si mauvais que certains le pensent.

Il faut reconnaître d'ailleurs que si l'on pousse les choses dans cette voie, le calcul du coefficient de consanguinité moyenne, comme test d'endogamie, peut se trouver transformé dans une certaine mesure. Les critiques qu'on peut en faire aussi dans le sens *Wahlund-Dahlberg* et *Wright* arrivent à poser que le meilleur moyen de calculer ce coefficient, est encore d'établir la généalogie de la population étudiée. Ce procédé permet en effet de supprimer un ensemble de considérations génantes: démographiques, sociologiques, institutionnelles, etc. Ici, on ne peut tricher puisque l'on a, sur plusieurs générations, la structure exacte des parentés et qu'on peut se passer des coefficients ou des généalogies

tronquées. Nous signalons dans une autre communication de ce congrès, sur les eskimos polaires, que le procédé est facile avec une méthode mécanographique et particulièrement utile à l'avenir pour les anthropologues et les ethnologues. En réalité, on ne voit pas comment les deux notions pourraient systématiquement s'opposer. La valeur de la mesure par les mariages entre cousins doit être indéniable dans certains types de population. Si l'isolat est strictement fermé et limité et si les unions s'y rapprochent du hasard, la mesure reste certainement valable. Sa valeur se justifie par les résultats brillants obtenus par la méthode sur les populations animales (escargots), *Lamotte* [1952]. Mais si le hasard ne joue pas, sa validité peut être mise en doute. Dans un cas comme dans l'autre, on peut penser que l'appréciation de l'évolution des isolats peut être estimée par la mesure de la distance séparant les lieux de naissance des enfants par rapport à ceux des parents ou, ce qui est plus accessible, par les domiciles des époux sur plusieurs générations. Il est possible encore que l'établissement de généalogies totales ou partielles, nous éclairent plus précisément sur ce problème important.

Nous avons voulu montrer rapidement ici que les modèles de la génétique formelle se heurtent dès maintenant aux réalités sociales et culturelles. On ne peut que s'en réjouir car, peu à peu, disparaît cet aspect théorique qui maintenait les rares recherches entreprises dans ce domaine dans une atmospère hautement spéculative. En se pliant à la réalité humaine de tous les jours, la génétique de population va rendre, dans un proche avenir, d'immenses services à toutes les sciences de l'homme.

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STRUCTURE DÉMOGRAPHIQUE ET GÉNÉTIQUE DE L'ISOLAT DES ESKIMOS POLAIRES (THULÉ, GROENLAND)

Par J. SUTTER et L. TABAH

Les eskimos polaires fixés dans le district de Thulé, sur la côte nord ouest du Grœnland (76–79° de latitude Nord) représentent la population la plus septentrionale du globe. En 1950–51, un explorateur français *Jean Malaurie* fit un long séjour au sein de ce groupe pour le compte du Centre national de la recherche scientifique. Il put rassembler une documentation démographique complète qui fit l'objet d'une étude spéciale, en collaboration avec nous-mêmes, en 1952.

Les principales caractéristiques démographiques de cette population sont les suivantes: le recensement nominatif de *J. Malaurie* donne 302 personnes vivantes: 146 femmes et 156 hommes. La nuptialité est très élevée. De 1940 à 1950, 116 naissances ont été enregistrées: 63 garçons, 49 filles et 4 morts-nés. Le taux de fécondité est de 173 pour mille. Ce taux paraît faible pour une population à forte nuptialité et ne pratiquant pas la contraception, mais il s'explique partiellement par une stérilité relativement élevée: 16% des femmes mariées sont stériles. Si l'on tient compte seulement des femmes fertiles, on s'aperçoit que le taux de fécondité est de l'ordre de 300 pour mille, ce que l'on observe généralement dans les populations non malthusiennes. Le taux brut de mortalité est de 27 pour mille, ce qui est, relativement, assez élevé car la population de Thulé est jeune. Les espérances de vie à la naissance sont de 28 ans pour les hommes et de 22 ans pour les femmes. Il existe donc une surmortalité féminine, alors que c'est le phénomène inverse que l'on observe dans presque toutes les populations étudiées à ce jour. Il existe une forte mortalité à l'âge adulte, qui a pour conséquence de nombreux remariages,

aussi bien chez les hommes que chez les femmes. La courbe de survie de la population de Thulé est très comparable à celle de *Duvillard* (France XVIII[e] siècle) et à celle de l'Inde (1901). L'étude du taux net de reproduction montre que le renouvellement des générations n'est assuré à Thulé qu'avec une faible marge de sécurité. Elle montre encore que la population de Thulé, qui persiste en s'accroissant faiblement, au rythme de 0,8 % en moyenne, s'est constamment trouvée dans une situation démographique précaire.

L'augmentation de la population eskimo de Thulé a été relativement beaucoup plus faible que celle des autres stations eskimos étudiées au Grœnland. En réalité, cette population pose le problème de la population minimum.

Les problèmes posés en génétique de population par la structure des isolats doivent a priori bénéficier de l'observation d'un groupe aussi fermé que celui de Thulé. Nous avions là l'occasion rare d'étudier en détail l'état de l'endogamie dans une population géographiquement isolée, numériquement réduite et où les migrations sont rares. Une population de ce genre semble devoir satisfaire au mieux les conditions de la panmixie, cet ensemble d'hypothèses sur lequel repose les modèles fondamentaux de la génétique formelle. On y suppose en effet que la population est fermée, que les mariages s'y font au hasard et que la fécondité est identique pour tous les couples. On pouvait donc étudier avec fruit, sur une population pour ainsi dire expérimentale, une série de problèmes primordiaux dont le moindre n'était pas de vérifier dans quelle mesure le nombre des mariages consanguins peut servir à estimer la dimension de l'isolat.

Mais la méthode classique pour étudier l'endogamie sur laquelle nous nous sommes à plusieurs reprises étendus rencontrait des difficultés dans son application pour deux séries de raisons principales:

a) Pour calculer le coefficient moyen de consanguinité de la population, on doit connaître le coefficient des couples qui ont engendré chacun des individus vivants. Il est donc nécessaire de connaître la structure de la parenté jusqu'à des degrés assez élevés. Or, la généalogie de Thulé, telle qu'elle a été recueillie par *J. Malaurie*, englobe suivant les lignes, trois, quatre ou, au mieux, cinq générations. On ne peut de la sorte connaître que les mariages du 6[e] degré dans le cas de quatre générations et seulement les mariages du 8[e] avec cinq générations, ce qui est court.

b) D'autre part, les institutions interdisent pratiquement à Thulé tous les mariages consanguins jusqu'au 6[e] degré. Ce fait joint à l'insuffisance des degrés rapportés par la généalogie rend inapplicable le mode classique de calcul. En effet, le coefficient moyen de consanguinité, calculé

dans l'hypothèse où les mariages d'un degré supérieur au 5e ont un coefficient nul, devient lui-même nul.

Nous avons donc été amenés, pour calculer ce coefficient, à utiliser une autre voie que celle employée habituellement. L'objectif est de connaître la fréquence des mariages des 7e, 8e, 9e et 10e degrés de consanguinité à l'aide de notre matériel généalogique.

Pour cela, nous avons considéré les individus vivants de Thulé âgés de 0 à 15 ans (124 au total, 62 garçons et 62 filles.) En 1965, ces individus auront de 15 à 30 ans et l'on dispose, en faisant le calcul à partir d'eux, d'une génération supplémentaire.

Imaginons que chaque individu appartenant à ce groupe y choisisse son conjoint et, dans deux hypothèses, calculons le coefficient moyen de consanguinité qui en résultera:

1. les mariages sont conclus au hasard, les seuls degrés de parenté qui empêchent l'union étant: frère-sœur, oncle-nièce et tante-neveu;

2. les mariages sont encore conclus au hasard, mais l'exclusion s'étend cette fois jusqu'au 6e degré de consanguinité comme on l'observe réellement.

Deux problèmes se posent alors. Quel degré de parenté peut-on accorder 1°) aux unions supérieures au 8e degré et, 2°) aux ancêtres communs ? Du fait de l'isolement, une certaine accumulation de consanguinité doit s'être produite à Thulé au cours du temps.

Nous avons finalement calculé les deux coefficients, en indiquant, pour chacun d'eux, une limite maximale.

Pour effectuer le calcul, on a tenu compte, pour chaque individu des différents âges de 0 à 15 ans, de la répartition des degrés de consanguinité le liant aux autres individus du groupe.

Comme on peut le voir en 1950, les cousins d'un individu du sexe masculin âgé de 0 à 15 ans se repartissaient en moyenne, comme il suit, selon les différents degrés: 3,53 du 4e; 1,78 du 5e; 4,15 du 6e; 1,76 du 7e; 0,33 du 8e et 0,47 du 9e. Il restait encore en moyenne 47,73 individus ne lui étant pas apparentés à aucun degré déterminé. Si l'on tient compte de la mortalité jusqu'à l'âge adulte, on peut estimer que, finalement, un individu pourra choisir son épouse parmi 32 personnes qui ne lui sont pas apparentées, ou, tout au moins, qui ne lui sont pas apparentées à un degré inférieur ou égal au 9e.

Voici les résultats des calculs effectués suivant les indications précédentes:

1. Coefficient moyen de consanguinité dans le cas où sont exclus les seuls mariages des 2e et 3e degrés (frère-sœur, oncle-nièce, tante-neveu),

en supposant que les mariages du degré supérieur au 6e ont des coefficients nuls, et que les ancêtres communs ont eux-mêmes des coefficients nuls: garçons: 0,0036, filles: 0,0035.

2. Coefficient moyen de consanguinité dans le cas où l'interdit porte jusqu'au 6e degré de consanguinité, en supposant que les mariages d'un degré supérieur au 6e ont des coefficients nuls et que les ancêtres communs ont eux-mêmes des coefficients nuls: garçons: 0,00023, filles: 0,00020.

3. Coefficient moyen de consanguinité dans le cas où sont exclus les seuls mariages des 2e et 3e degrés, en supposant que les unions de degré inconnu et celles des ancêtres communs ont un coefficient correspondant à une union du 10e degré: garçons: 0,0066, filles: 0,0064.

4. Coefficient moyen de consanguinité dans le cas où sont exclus les mariages des 2e et 6e degrés, en supposant que les unions de degré inconnu et les ancêtres communs ont un coefficient correspondant à une union du 10e degré: garçons: 0,00320, filles: 0,00302.

On voit donc que le coefficient moyen de consanguinité de cette population doit être compris entre 0,0002 (hypothèse 2) et 0,0030 (hypothèse 4).

Finalement, le chiffre vraisemblable est relativement faible. Il montre que dans les populations très réduites du point de vue du nombre et les plus fermées aux mouvements migratoires, *il suffit d'exclure tous les mariages jusqu'au 6e degré pour éviter une réelle augmentation de la fréquence de l'homozygotie.*

Du point de vue des recherches à entreprendre, il apparaît qu'il n'est pas nécessaire de remonter dans les chaînes de parenté à des millénaires, mais qu'il faut posséder parfaitement au moins 4 générations. La connaissance de 5 générations doit suffire largement.

Les résultats précédents étonneront plus d'un spécialiste. On pouvait penser, en effet, en examinant le résultat de recherches analogues effectuées jusqu'ici sur des populations assez diverses, qu'un isolat comme celui des eskimos polaires devait manifester un degré d'endogamie prononcé, bien exprimé par un coefficient moyen de consanguinité d'une valeur certainement élevée. Voici, à titre documentaire, quelques chiffres – multipliés par 10000 – rassemblés récemment par *A. J. Böök*: Pour des paroisses du Brésil au milieu du XIXe siècle (*Freire Maia* [1952]) ~ 11, ~ 35, ~ 44; Archidiocèse de Vienne 1901-1930 (*Orel* [1932]) ~ 6; France toute entière 1926–45 (*Sutter* et *Tabah* [1948]) ~ 7; Caste des Parsis et des Marathes (*Sanghvi* [1954]) ~ 92, ~ 75; Indiens Ramah Navaho (*Spuhler* et *Kluckhohn* [1953]) > 66; Paroisses suédoises 1890-1946 (*J. A. Böök* [1956]) ~ 8, ~ *24*, > 58, etc.

Nous voyons que le coefficient des eskimos polaires est relativement

faible comparé à ces chiffres. Cette constatation est pleine d'enseignements et on pourrait la commenter longuement si l'on n'était limité par le cadre restreint de cet article. Ce qu'on doit retenir d'essentiel c'est qu'une population numériquement très réduite et fermée aux mouvements migratoires comme celle-ci, échappe à l'endogamie profonde et à ses conséquences génétiques grâce à ses institutions.

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SOME NOTES ON THE BREEDING PATTERNS OF HUMAN POPULATIONS

By L. L. CAVALLI-SFORZA

A research plan was inaugurated in an area of the province of Parma, Italy, with the object of analyzing a standard European population showing a wide gradient of geographical, historical, social and economic conditions, on which demographical data of genetic interest are available. While it will take some time to carry out the whole research plan, I hope it may be of interest if I give a report of some results which have been obtained since the beginning of the investigation.

The standard analysis of breeding patterns by the study of consanguineous marriages has been carried out, due consideration beeing given to the village size and ecology. As an index of ecological conditions at large, the height above sea level was used in view of its high correlation with any other parameter of importance for the natural history of this population.

Table 1 shows the number of parishes having given census and altitude. It is clear that village size is reduced with increasing height above sea level (the town of Parma is not included in the table). The same table shows, on the right, that average consanguinity (calculated from the frequency of consanguineous marriages in the years 1927–51 with con-

sanguinity degrees between $^1/_8$ and $^1/_{64}$) depends not only on village size but, within each class of village size, also on altitude. There is, as might be expected, more consanguinity in the more isolated villages.

Table 1. Consanguinity in Parma Diocese. Distribution According to Village Census and Altitude.

	Number of Parishes				Average consanguinity ($\times 10^3$)		
	Altitude (metres)				Altitude (metres)		
Census	0–299	300–699	700–1100	Totals	0–299	300–699	700–1100
0– 299	15	27	30	72	1.88	2.04	3.69
3– 599	39	42	14	95	0.52	0.93	1.75
6–1099	44	18	5	67	0.57	0.75	1.49
11–5000	34	3	2	39	0.41	0.65	2.16
Totals	132	90	51	273	Town: 0.31		

Table 2. Percentages of First Cousin Marriages.

	Village altitude					
Census	0–299	300–699	700–1100	Average	Isolate size	Average Village size
0– 299	2.4	2.0	2.5	2.28	238	199
3– 599	.4	.7	1.1	0.67	809	440
6–1099	.7	1.0	.4	0.81	670	820
11–5000	.5	.8	1.4	0.57	1060	1960
Average	0.6	1.0	1.5	0.77	706	690

Table 3. Percentages of Second Cousin Marriages.

	Village altitude				Only for altitude > 700 metres	
Census	0–299	300–699	700–1100	Average	Isolate size	Average Village size
0– 299	1.8	2.7	8.1	4.7	297	193
3– 599	.7	1.7	5.0	1.7	482	415
6–1099	.4	1.3	5.4	.9	446	690
11–5000	.4	.4	4.3	.6	560	1500
Average	.5	1.6	6.0	1.25	417	354

It is of interest to analyse in detail the origin of this greater consanguinity. Table 2 and table 3 show, respectively, the distribution of first and of second cousin marriages according to village size and altitude. For first cousin marriages the census effect is more important than the effect of altitude. If one calculates isolate sizes with the standard formulas given by *Dahlberg* one finds values fairly close to the actual village sizes, except that they are higher than those for the smaller villages, and smaller for the larger ones. It should be stressed, however, that the

agreement must be partly coincidental. They are taken here to have essentially formal value.

The distribution of second cousin marriages shows another pattern. Although village size has also here a clear-cut effect, altitude plays now a major rôle. When villages of the highest altitude are used for estimating isolate sizes, the figures observed are practically superimposable with those obtained from first cousin data.

The discrepancy between first and second cousin data is likely to be due to differences in migration rates as affected by the different ecological and social conditions. Assuming that immigration is exactly balanced by emigration it is possible to estimate the fraction x of population exchanged per generation, assuming it to be zero for the highest villages. From first cousin data, x turns out to be 33% (1–1.0 1.5) in the medium high villages and 60% (1–0.6 1.5) in the lowest villages. Estimates from second cousin data may be obtained taking into account the fact that migration may have taken place over two generations instead of one. This fact may explain the more marked effect of altitude on second cousin as compared with first cousin data. Values thus estimated from second cousin data are 48% and 71% for medium high and low villages respectively, thus comparing favourably with the above.

Although good migration data have not yet been obtained, it is probable that the migration rates as given above are overestimated, possibly because immigration exceeds emigration in the lower areas.

One way of estimating migration that has been used shows however that, qualitatively, the picture must be correct. This was done by the analysis of surname turnover. In a mountain village of 145 people, only 10% of the people living nowadays have a surname which was not present in the village 300 years ago. But in a typical village of the plains it has taken only 68 years to have 50% of the people carrying a new surname not formerly represented. This means a turnover rate approximately thirtyfour times greater in the plains than in the mountain village considered, but this method underestimates the population exchange due to women marrying and establishing themselves in another village, which, in the mountain range at least, is more frequent than the reverse.

Parish books of marriages offer another type of analysis of migration that can be traced back for three centuries or more, viz. the estimation of the frequency of marriages with at least one member coming from another parish, and of the distances of the origin of mates. Out of 298 marriages celebrated in a mountain village over 300 years, 40% were between mates, one of whom was alien to the village (usually, the brides).

The distance from which the alien mate came was not, on average, much above 8 kilometres.

There is no great difference between the patterns thus observed between mountain villages and villages in the plains, but this mode of analysis is rendered difficult by the fact that the parish chosen for celebration of marriages is not the best one from the point of view of genetic analysis, which would be that of future residence of the married couple.

I would like to report of another way of estimating migration. It is a laborious one but may be rewarding for some particular aspects of evolution in partially isolated populations, which have not been considered so far.

Table 4. Fertility of Marriages (*Riana* [1650–1900]).

Mates born in parish	Consang.	Progeny size 0	1	2	3	4	>4	Sum	Mean	Variance	Diff. bet. means
Both	Yes	22	16	14	7	–	–	59	1.10	1.09	t = 0.8
	No	21	32	20	10	4	–	87	1.36	1.23	(P > 5 %)
	Total	43	48	34	17	4	–	146	1.25	1.18	t = 2.3
One only	–	20	24	28	6	4	4	86	1.67	2.86	(P < 5 %)
Grand total		63	72	62	23	8	4	232	1.409	1.836	

Church books can be used to estimate the fertility of marriages by examining at least one full generation cycle, e.g. by counting the number of children per family who marry and take residence in the same village after marriage. In table 4 the distribution of fertilities is analysed over a period of 300 years for a mountain village, and a comparison is made between marriages according to the origin of mates, i.e. whether they are both born in the same parish ("home" marriages) or one of them at least comes from other villages ("cross" marriages). Consanguinity is also partially taken into account, although the sample analysed was not sufficient to show significant differences.

The method of estimation, by counting potentially fertile progeny, takes into account both social and biological factors, and gives a satisfactory estimate of the fitness of a marriage. By this method, the fertility of cross marriages turns out to be, in the village examined, 34% higher than that of home marriages; the difference, 1.67 versus 1.25 is statistically significant (table 4). The introduction of foreign genes into the village by alien mates is thus more important than would be gathered simply by counting the alien mates themselves. The difference does not seem to depend entirely on the fact that consanguineous matings are more frequent among home marriages; in fact, non consanguineous home marriages have a fertility of 1.36, lower (though not significantly so) than

that of cross marriages (1.67, including only a few consanguineous marriages).

Thus outbreeding seems to play a role more important than the mere count of foreign parents would imply. This phenomenon is not surprising; on the contrary it could be expected, as the following considerations show, and it is likely to be more prominent with communities smaller than the present one (a village of 145 people) such as those that might be encountered, e.g., in primitive populations.

It is well known that in a population fragmented into a number of small isolates, each isolate will tend to show inbreeding, and it is said that gene frequencies in the isolates will drift from the original ones. But, if isolation is partial, immigrants to the village (who will have gene frequencies close to those of the general population) marrying with local people, will have progeny more frequently heterozygous than the progeny from home marriages. More generally, their progeny will have gene frequencies midway between those of the local population and those of the population as a whole and if the latter is at equilibrium in respect of selective forces, such progeny will have fitness higher, on an average, than that of local people.

A consequence of this should be considered. If genes for which a polymorphism exists happen to be, in the period of time considered, almost devoid of selective value, so that they might more easily drift away in an isolate, they will be affected by the increased fertility of cross marriages exactly as much as the genes which are responsible for it. The effect will be lost after the first generation (being renewed only by new migration) for genes having no selective value of themselves, unless they are linked with genes under selective pressure, in which case the effect will persist longer. Genes which are not under homeostatic or, in general, selective pressure will thus borrow homeostasis, or selective value, from the genes that directly contribute to the selective effect, and thus in a partially isolated population the selective value of an individual gene loses its significance, at least to a degree, and with a strength proportional to that of isolation itself.

One may thus expect the stabilizing effect of migration on gene frequencies in partial isolates (subject to similar selective forces) to be higher than might be expected from crude migration data. The increase is bound to be higher the stronger isolation is, while to a certain degree it is independent of the selective forces to which the individual genes examined are exposed, being rather dependent on the total homeostasis, or, in general, the total of the selective forces to which the population is exposed.

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THE PHYSICAL ASSIMILATION OF THE DESCENDANTS OF IMMIGRANTS

By C. GINI

In South Italy, there are remnants of many foreign groups who settled down there several centuries ago: Albanians, Slavs, Greeks, Gipsies, Provencals, Valdensians. At the close of the last century a large-scale anthropometric enquiry was made in Italy by the Ministry of War on the soldiers of the age groups born in 1859–63 doing military service; among other things, returns were made for the cephalic index, the stature and pigmentation of each soldier. The data obtained show that no trace of the characteristic features that the ancient immigrants may be supposed to have had, has been found in the population.

Does this assimilation, seemingly complete, of said physical characteristics depend only on the mingling, that must certainly have occurred in a certain measure in the elapse of time between the foreign groups and the autochthonous inhabitants, or is it also due to the influence exercised by the environment? This is the first question.

Its study can be made best on the settlements of the Albanians, both because they are more numerous, and because in many places they still preserve their language, their traditional costumes, and other cultural characteristics that bear witness to a greater degree of isolation, and because the Albanians, who are tall and markedly brachicephalous, differ more strikingly as regards the cephalic index and stature from South Italians. These settlements have therefore been the subject of inquiries made by the Italian Committee for the Study of Population Problems (C.I.S.P.) under the direction of the author. Among the Albanian settlements the three especially isolated villages of Carfizzi, S. Nicola dell'Alto, and Caraffa in Calabria were selected, whose population differs most markedly from the Albanian type because of its low cephalic index and

low stature. A research group of scientists intending to solve this problem, carried out in 1938 not only the measuring of the anthropological features of individual persons, but established also, by means of patient questioning and control, whether their ascendents belonged to the foreign or the autochthonous population, so as to be able to classify the inhabitants in groups of purely Albanian blood or completely Calabrian, or of mixed blood in which the Albanian element prevailed or of mixed blood in which the Calabrian element prevailed.

The results referring to 84 anthropometric characteristics of the adult males and 83 of the adult females of the villages above mentioned show that there was no appreciable difference as between the several groups of inhabitants classified according to the percentage of foreign or autochthonous blood. This justified the conclusion that the essential cause of physical assimilation is to be found not so much in the mingling of the groups as in a direct or indirect influence exercised by the environment.

Beside the ancient foreign country settlements, we have in South Italy settlements of North Italians and more especially of Ligurians in Sardinia in the Island of Carloforte, and mixed with Piedmontese, in the commune of Calasetta which lies opposite Carloforte, while yet older settlements of Piedmontese had been formed in Sicily. Now, while no appreciable traces of the remoter Piedmontese immigrants were found in the data of the soldiers of the age groups born in the years 1859–63, on the other hand the data point to a well-defined differentiation from the surrounding Sardinian population in the case of the Ligurian settlement of Carloforte and of the Ligurian-Piedmontese settlement of Calasetta. It should be noted that these two settlements are more recent, the earliest arrivals dating from the middle of the eighteenth century, and they conserve intact the language, the habits, and the original cultural inheritance of Liguria (the Piedmontese elements in Calasetta having been absorbed by the Ligurians) so that they represent real and proper Ligurian cities in Sardinian territory.

In 1939 and 1940 other scientific expeditions were arranged by the C.I.S.P. to study these settlements. Again the individuals examined were classified according to the percentages of foreign and autochthonous blood. The physical characteristics of the adults of Carloforte and Calasetta were found to differ from those of the Sardinian population and, except for fluctuations depending on disturbing circumstances, the difference was generally more marked if the percentage of foreign blood was increased. These differences were, however, much less marked than those noted for the soldiers of the age groups born in the year 1859–63, nearly

half a century ago, and in the case of pigmentation, for which the comparison could be made, it was less marked in the case of babies and children examined in the seaside holiday camps and when they left the church services, than in that of adults. It was therefore evident that a progressive assimilation was taking place.

Two more expeditions were organised by the C.I.P.S. in 1952 to Carloforte and in 1953 to Calasetta, and the data obtained, when compared to the similar data returned in the previous enquiry, suggest that in the thirteen years interval there has been a darkening of the pigmentation, which confirms the progressive assimilation of the foreign settlers to the Sardinian type.

The process of assimilation is less advanced at Calasetta than at Carloforte, which can be explained by the fact that at Calasetta, where practically all the residents are agriculturists, the differential reproductivity of the social classes has less importance than at Carloforte, where it plays a part in the progressive assimilation.

Now, in which way is the assimilation taking place ? This is the second question. In view of contributing to its solution 451 families at Carloforte and 390 at Calasetta were examined one by one in the enquiries of 1952–53, noting the pigmentation of their present members and that of the members of the previous generations.

Our attention was attracted by two facts. One is the frequency with which parents with blue or green eyes without any appreciable trace of brown pigmentation have children with mixed or brown eyes.

The second fact concerns the darkening of the hair with advancing age, a fact indeed which is of common observation in many populations, but which seems to assume at Carloforte and Calasetta an exceptional frequency. The local population, which has noted it, thinks it is influenced by the sea air, an explanation in favour of which I see no confirming facts or arguments. At Calasetta as well as at Carloforte the opposite change is sometimes observed, but with a much lower frequency: children are born with dark hair which after a certain time, suddenly or gradually, becomes lighter. Some more complicated changes also occur, although exceptionally. The children of the same family, in the majority of cases, differ from this point of view, some of them presenting a progressive darkening of hair as they grow older and others on the contrary preserving the colour shade they had at birth. This fact is important in as much as it shows that the darkening does not depend—or at least does not depend exclusively—upon the influence of external factors during individual development, but partly at least upon inborn factors.

The data collected are in course of elaboration.

In the meantime some conclusions seem authorised:

A. After about 5 centuries, foreign settlements of immigrants, differing so widely from the local population as the Albanians from the Calabrians, have been assimilated in a practically complete manner.

B. The assimilation seems, at least for a substantial part, not to be due to the mingling of stocks, but to an influence, direct or indirect, of the environment.

C. The experience of the Ligurian and the Piedmontese colonies in Carloforte and Calasetta suggests that the physical characteristics of the immigrant stock may victoriously resist the influence of the environment for a long while, as it has been the case for a century or a century and a half at Carloforte and Calasetta, but subsequently the resistance weakens, and the assimilation gradually takes place.

D. The influence of heredity and accidental mutations on the physical characteristics of the populations are obviously not to be denied or undervalued, but it is certain that the aforesaid results seem, at first sight, to contrast with the overwhelming influence of heredity rather than environment, pointed out by researches on human twins. The contrast however is only apparent, as the researches on twins show the relative influence of heredity and environment from one generation to another. Now the direct and indirect influence of environment is, at least in part, cumulative through the generations, while nothing similar seems to exist for heredity. Thus only in a long time the full influence of environment manifests itself and becomes overwhelming over that of heredity.

E. In contrast with the current opinions of students of anthropological sciences and perhaps also of students of social sciences, the cultural tradition may be more tenacious and persistent than physical heredity. Populations completely or almost completely assimilated from the physical point of view, such as the Albanians of Calabria, still preserve a remarkable part of the original culture characteristics; while populations which preserve in full, or almost so, the cultural heritage of the country of origin, such as the Ligurians of Carloforte and Calasetta, offer, after a certain number of generations, a notable and probably progressive attenuation of their original physical characteristics.

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The physical assimilation of the foreign settlements in Italy. Report presented in Italian and English language at the 9th Int. Congr. of Genet., Bellagio 1953, and reproduced in Acta genet. med. Gemell. *3*, 3, 1954.

Discussion

G. Montalenti (Napoli): Have the blood group frequencies been considered in the more recent investigations?

C. Gini (Rome): The OAB blood groups have been examined for all the individuals, but, as their distribution does not show marked differences between Calabrian and Albanian as well as for Ligurian or Piedmontese and Sardinian or Napolitans their examination cannot be useful for the racial discrimination. The other blood groups were not examined. (The examinations have been made in 1938 for the Albanian and, mainly, in 1939—1940 for the Ligurian or Ligurian-Piedmontese colonies.)

Gini, C.: Acta genet. *6*, 404–406, 1956/57

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THE EXTINCTION OF THE NORSE SETTLEMENTS IN GREENLAND

By C. GINI

The author, as founder and president of the Italian Committee for the Study of Population Problems, which has in its program the study of the isolated ethnic groups, has given special attention to the extinction of the Norse settlements in Greenland which offer a conspicuous example of an ethnical group which has died out for reasons that so far are spoken of as a mystery.

As far back as 985 or 986 a group of Norse settlers, under the leadership of Erik the Red, reached Greenland, where they formed two colonies

on the Western coast, called respectively Western and Eastern Settlement. The Western Settlement had ceased to exist about 1350, while the Eastern one still showed signs of life about 2 centuries later. This paper treats especially of the extinction of the Western Settlement.

Many causes have been adduced for the extinction of the two settlements, without making a distinction between them: destruction by the Eskimos, raids by pirates, deterioration of the climate, economic impoverishment, emigration, physical degeneration; but, if they may have slowly corroded the Eastern Settlement, none of them throws light on the disappearance of the Western one which occurred before those phenomena had made themselves felt or had time to lead to important results.

Moreover the skeletons exhumed from the burying grounds of the Western Settlement show no signs of physical impoverishment, while there is no record of struggles between Norse and Eskimos before the disappearance of the said colony and, moreover, according to a version accepted by the Roman church, its settlers had voluntarily been converted to the American (i.e. Eskimo) faith.

The author suggests, that the disappearance of the Western Settlement has been facilitated, if not determined, by the marked disproportion between the sexes, as shown by its skeletons.

The figures are very small (26 female skeletons versus 12 males), but the regularity with which the proportion of females increases from the oldest to the youngest skeletons, i.e. roughly from the more remote to the more recent generations, is impressive: 50 females to 100 males among the skeletons of persons between 50 and 60 years of age; 116 per cent among those between 40 and 50 years; 200 per cent among those from 30 to 40; 500 per cent among those from 25 to 30, 1000 per cent among those from 20–25, only one female and no male from 18 to 20.

This progressive disproportion of the sex-ratio must strongly have reduced the birth rate, as it happened at the end of the 19th century among the Samaritans of Palestine, where the scarcity of females seriously endangered the survival of the community.

Among the Norse settlers the serious lack of men must have let the women willingly mix with the Eskimos and eventually abandon the colony.

This explains why, according to a contemporary evidence, the colony abjured the Catholic faith and accepted the Eskimos' religion and customs. An expedition especially organized in the middle of the 19th century by the heads of the Eastern Settlement, evidently alarmed by news they had received, found the Western Settlement deserted, large

numbers of cattle left to themselves and no trace of either Christians or pagans, i.e. either of the Norse settlers or of the Eskimos.

Evidently the settlers, the great majority women, had emigrated, leaving behind, at least to a great extent, the cattle, formerly looked after by the men and foreign to the Eskimo culture.

Also the findings of the recent excavations of the ruins are highly suggestive as they show a great abundance of the objects which are foreign to the Eskimo culture (shoe lasts, spindles, spindle-whorls, trenchers, combs of Norse fashion) while hunting and fishing weapons, footwear, furs and personal garments and ornaments, vessels were scarce or absent. It is true that these objects would have been taken away by the Eskimos, had they destroyed the settlement, but in that case, it is certain that all the cattle would have been killed.

Moreover, those objects left behind are often found not in the houses but in the stables and this gives the suggestion that the women, having already assimilated the customs of the Eskimos, has put them aside and shut them up in the stables, the doors of which had probably been opened for the cattle to go out.

The causes of the extinction of the East Settlement may have been different. The skeletons exhumed from their grounds do not suggest any scarcity of males. It is probable that the main group of their settlers suffered from the fighting with the Eskimos of which the Norse chronicles as well the Eskimos traditions bear record, while the farms of Herjolfnes, located further South and standing apart, may have been unaffected by such struggles at least for long and, favored by the position, lasted until the isolation actually determined the racial impoverishment that is shown by their skeletons.

Discussion

C. L. Vebæk, (Copenhagen): I regret that so little time was at the disposal of the lecturer for this interesting paper, and that accordingly it had been necessary for the lecturer to cut it down considerably. Professor *Gini* had, however, kindly let me read his manuscript beforehand so that I had been able to study it in detail. Professor *Gini*'s lecture and the hypothesis he had set forth was of the greatest interest to Danish archaeologists studying the medieval Norse culture in Greenland, but we were regrettably unable to accept this hypothesis and Professor *Gini*'s proofs in favour of it. In our opinion the Eskimos had destroyed the Western Settlement. This has certainly not yet been definitely proved, and although we were unable to agree with Professor *Gini* we would, of course, take his hypothesis into consideration.

C. Gini (Rome): There is no doubt that the Eskimos had an important rôle in the disappearance of the Western settlement, if they took with them the Norse women. On

the other hand the fact that the cattle had been left behind proves, as *Nansen* has remarked, that the settlement had not been sacked, otherwise the Eskimos would certainly have killed the cattle up to the last one. And we must not forget that the Norse chronicle speaks of a peaceful acceptance of the Eskimos' faith and costums by the settlers of the Western colony, and the Roman Church, who obviously was not interested in supporting that version, has accepted it.

Oostingh, R.: Acta genet. *6*, 407–409, 1956/57

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RELIGIOUS FACTORS IN ISOLATE FORMATION

By R. OOSTINGH

With regard to religion, the Netherlands show a miscellaneous picture: 35–40% of the population are Roman Catholics, 60–65% are non Roman Catholics, Protestants of different groups. In this communication two groups are considered viz. Roman Catholics and Protestants; in the second group the non religious part of the population is included.

In the southern provinces the Roman Catholic religion prevails, in the northern provinces (Groningen, Friesland and Drenthe) the Roman Catholics form a small minority of the population.

In a small municipality in the north of Groningen a general practitioner practices in a population composed of two parts, a Roman Catholic and a Protestant. To a certain degree one can speak of a R.C. enclave in a Protestant region.

The general practitioner obtained the impression that the two groups suffered from a different "pattern" of diseases. He decided to test his impression by means of a personally executed inquiry with 500 R.C. persons and 1100 Protestants.

For the present it can be said that the groups differ significantly with regard to the total incidence of diseases. This part of the investigation has, however, not been finished.

A number of normal characters have been included in the investigation, viz. the bloodgroups A.B.O., M.N., Rhesus, the secretor factor and the testing of P.T.C. in different concentrations.

200 persons of each have been examined.

A. B. O. bloodgroup.

	A.	O.	B.	A.B.
Roman Catholics . .	36 %	53 %	6 %	4,5 %
Protestants	45,5 %	43 %	8,5 %	3 %

gen frequencies	A.	0.	B.
R.C.	0.215	0.728	0.043
Pr.	0.285	0.655	0.065

M. N. bloodgroup.

	M.	N.	MN.
Roman Catholics	44 %	15,5 %	40,5 %
Protestants	25,5 %	22,5 %	52 %

gen frequencies	M.	N.
R. C.	0,642	0,358
Pr.	0,515	0,485

Rhesus bloodgroup.

	C.	c.	D.	d.	E.	e.
Roman Catholics . .	66 %	34 %	83 %	17 %	22 %	78 %
Protestants	63 %	37 %	82 %	18 %	32 %	68 %

The R.C. group shows a distinct higher frequency of the O gen.

The R.C. group shows a distinct higher frequency ot the M.gen.

The number of persons with genotype cde cde appeared to be 17.5% with the R.C. group, 15.5% with the Protestant. The difference between the groups is rather small.

Secretor factor

This character has been examined with 94 R.C. and with 114 Protestant people. In the first group 72% appeared to be secretor, in the second 78%; the difference is not significant.

Tasting P.T.C.

It is known that the result of the experiment of testing P.T.C. cannot be explained by one inheritance factor: the concentration excercises some influence as well as the sex of the testee.

For this experiment 3 concentrations have been used: 1/32%, 1/128% and 1/512%.

Testers	1/512 %	1/128 %	1/32 %
Roman catholics	37 %	51 %	58 %
Protestants	62 %	76,5 %	80,5 %

There is a distinct difference between the groups: the percentage of testers among the R.C. group is clearly lower than among the Protestant. Women appeared to test in a higher percentage than men.

There are sound historical grounds for stating that both groups of the population are of the same origin. During the reformation in the 16th century one part of the population became Protestant while the other part remained Roman Catholic.

Several data have shown that so called mixed marriages between the groups were very infrequently contracted. The R.C. group contracted marriages either within the small community of the enclave or at greater distances (sometimes foreign countries: Germany). The first possibility increased the percentage of consanguineous marriages in the R.C. group (5th–8th degree incl.): ± 20 %, very highly compared with the Protestant group: ± 1 % (4th–8th degree incl.). The second possibility caused 28 % of the R.C. marriage-partners to be sought at a greater distance (22 % of the Protestants). On one side therefore inbreeding occurred while on the other side importation of genes from other populations took place.

It was not possible to complete this study and to draw definite conclusions. There is strong evidence that isolate formation caused by religious factors is concerned here.

Discussion

N. Freire-Maia (Paraná, Brazil): Regarding the two factors proposed to explain the differences found between the isolates analysed, I wish to point out that inbreeding, even at the highest levels, although producing changes in genotype frequencies, does not result in changes in gene frequencies. Perhaps differential emigration and genetic drift (provided at least one of the populations have been sufficiently small) could be invoked as the main causes.

Witkop, C. J.: Acta genet. *6*, 410–412, 1956/57

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A STUDY OF TRI-RACIAL ISOLATES IN EASTERN UNITED STATES

By C. J. WITKOP

There are known to exist in the eastern part of the United States some 28 well defined tri-racial isolates. These groups represent gene pools of various proportions of Caucasian, Negro, and American Indian races. These groups are known as mixed bloods in their own communities. They are not accepted into the white community and do not consider themselves Negroes. As a result, they maintain their racial integrity by in-marriage within a few family names. They all represent the remnants of eastern Indian tribes.

A preliminary survey of each group was made by a questionnaire letter to the county health officer in whose district these groups reside. On the basis of subsequent studies it has been shown that about 10% of the genetically determined conditions that actually exist in these groups are reported by this method. One of these groups was selected for a detailed genetic study.

Detailed Study

A detailed study of the medical, dental, mental health, and social aspects of one of these groups comprising 5 000 living members is in progress in southern Maryland. We are trying to determine all of the hereditary pathological traits present in the group. This group was selected for study for the following reasons:

1. This group marries for the most part within only 14 family surnames. 2. Records indicate that the group has in-married for nearly 250 years. 3. These people reside in a limited geographic area of 2 counties of

Maryland and the District of Columbia. 4. There are good records on births, deaths, and marriages of these people dating from 1741. 5. These people have the diseases which are being studied by National Institutes of Health. 6. Many types of matings rare in human material occur here.

The detailed study is divided into three phases:
1. Medical, dental and social histories are obtained from each individual by public health nurses. From this material, a census and pedigree is made. The pedigree information is verified from church records. All hospitalizations are checked and verified from the hospital records. 2. Dental, medical, ophthalmological and neurological field examinations are made of each individual. At this time bloods, urines, and salivas are collected from each patient and a P.T.C. taste test given. 3. Selected patients are brought to the National Institutes of Health for detailed clinical studies.

Each subject is being blood typed with 26 blood antigens. Electrophoretic patterns will be obtained on the hemoglobins, and a lipid analysis made of the plasma fraction. The urine specimens are being screened for tyrosene intermediates. Secretor factors are being determined from the salivas. Other special procedures are utilized where indicated by specific disease conditions. All data are being coded on I.B.M. cards to facilitate analysis.

This study has been in progress for one year. In the first 2,200 individuals for which we have some sort of information 18 genetically determined pathological traits have been definitely diagnosed. This does not include questionable cases that have yet to be examined.

Combinations of Traits and Anomalies

Some individuals in this study have shown combinations of several traits. Four patients have lop ears and dentinogenesis imperfecta. An albino has polycystic kidneys. A three year old boy with dentinogenesis imperfecta died with *Eisenmenger*'s complex. Two women with schizophrenia have dentinogenesis imperfecta. One child has deaf-mutism, dentinogenesis imperfecta, lop ears, and mental deficiency.

In most of the instances we have been able to show the independent inheritance of these conditions from different lines of predecessors. The occurrence of these conditions in one individual is most likely due to chance combinations of independent traits and does not represent a syndrome.

Reproductiveness

The reproductiveness of the people as a group does not seem to be impared. The average woman in this group had 5.7 offsprings during the years 1900 to 1950.

Isolates of the type presented represent prime examples of sociological factors influencing the prevalence of genetic disease conditions. Today in some of these groups, the genetic factors also influence the sociological factors, for while these groups were first isolated from the rest of the community on a racial basis, they are now partially isolated on a genetic basis. Many members of the community who might otherwise qualify as acceptable marriage partners have stated that they would not marry into the group because of the numerous genetic defects in these populations. Because of the length of time that in-marriages have taken place, these people approach an ethnic entity. It is perhaps through such groups as these that various racial strains had their origins in the past.

Discussion

F. DeMarinis (Cleveland, Ohio): How do you know that these groups are tri-racial? *C. J. Witkop:* From records both local and national dating back many years. Many studies have preceeded this work especially demographic and anthropological studies by Dr. *Calvin Beale* of the Census Bureau, Dr. *W. H. Gilbert* of the Indian Section, Library of Congress, and Dr. *Price* a social anthropologist of California.

Lehmann, H.: Acta genet. 6, 413–429, 1956 57

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VARIATIONS OF HAEMOGLOBIN SYNTHESIS IN MAN

By H. LEHMANN

Adult and foetal haemoglobins

It is exactly 90 years ago that *Körber* reported in his inaugural lecture at Dorpat University on a difference between the haemoglobin of the newborn infant and that of the adult. He had noted that "foetal haemoglobin" (now abbreviated to haemoglobin F) was resistant to destruction by alkaline reagents which rapidly denatured adult haemoglobin (haemoglobin A). Haemoglobin F normally disappears from the infant's circulation within 4 to 6 months. Its production is under a different genetical control from that of haemoglobin A.

The finding of haemoglobin F after the age of 6 months must be considered abnormal. It is known that it can be present after that age in a variety of conditions notably in anaemias which are caused by an inherited impediment of haemoglobin A production. Thalassaemia and sickle-cell anaemia are two such conditions where the finding of haemoglobin F is almost part of the diagnosis. Haemoglobin F can also be found at ages when it has disappeared normally in some cases of leukaemia, of spherocytic anaemia—where the abnormality is one of red cell shape and not associated with an abnormal haemoglobin—and even in children suffering from malnutrition. It thus seems that haemoglobin F may persist when an anaemia begins at an age at which the faculty of haemoglobin F production has not yet been lost. Such an assumption would explain why haemoglobin F is an almost regular feature in the haemoglobinopathies, but that it can also be seen in other blood dyscrasias

which are not necessarily inherited but acquired. Haemoglobin F itself should not be considered a cause of anaemia, but its presence after the age of 6 months should be taken to indicate an anaemia with an early onset in life.

The Haemoglobinopathies

An inherited abnormality of haemoglobin A production is called a haemoglobinopathy. There may either be a difficulty in producing the required amount of haemoglobin A, or haemoglobin A may be replaced by one of its variants such as sickle-cell haemoglobin (haemoglobin S), haemoglobin C etc.

Thalassaemia

In thalassaemia there is interference with the expression of the gene responsible for haemoglobin A formation. The homozygous condition results in a severe anaemia and death usually intervenes before adolescence. The clinical picture and the laboratory findings show much similarity with those seen in iron deficiency anaemia. However in this latter anaemia haemoglobin A formation is inhibited by the difficulty of finding iron to produce enough of the ironporphyrin prosthetic group, and the condition can be successfully treated when the deficiency is made good by iron therapy. In thalassaemia the materials for haemoglobin A production are all present but the erythroblast cannot make use of them. Thus an anaemia results which is almost identical with that seen in iron deficiency, except that there is no poverty in iron. The bone marrow is rich in iron deposits, and the serum iron level is normal or even raised. The determination of the serum iron level is a useful test in the differential diagnosis of the two conditions. Homozygous thalassaemia is called thalassaemia major, and the heterozygous thalassaemia is named thalassaemia minor. There is a wide variation in the clinical picture of thalassaemia minor. In some phenotypes the presence of one thalassaemia gene may cause so little disturbance that the diagnosis can only be made by family study. In most there is some hypochromia, poikilocytosis, and leptocytosis. The flat cells can be recognised as "target" or "mexican hat" cells, the decrease in mean cell thickness can be measured by direct methods or it can be inferred from a raised resistance of the red cells against lysis by hypotonic saline solutions. Some haemoglobin F is usually present. At the other end of the scale is the thalassaemia heterozygote where the penetrance of a single gene causes a condition resembling thalassaemia major. Family studies may be required to prove that the

patient is not a homozygote. All shades of thalassaemia minor can be found among the offspring of the same parent.

The thalassaemia gene and that responsible for haemoglobin A are under an independent genetical control.

Variants of haemoglobin A

Whereas the production of haemoglobin A is suppressed in thalassaemia, a variant replaces the normal pigment in the other haemoglobinopathies. Unlike haemoglobin F these variants do not differ from haemoglobin A by a resistance to alkali, or by their ultraviolet spectrum, nor indeed do any of them differ in their visible spectrum—though it is possible that a familial methaemoglobinaemia described on one occasion by *Hörlein* and *Weber* in 1948 forms an exception. The haem part of all known human haemoglobins is the same, and the differences are in the constitution of the globin. Some variations in amino-acid content have been reported. It is more likely that the fundamental differences will be found in the structure of the polypeptide chains, the number per molecule of titrable SH groups, of ionisable carboxyl groups etc. It is likely that the variants of haemoglobin A known up to date are allelomorphs, but so far this has only been established for the sickle-cell haemoglobin (haemoglobin S) and for haemoglobin C.

The first observation of sickle shaped cells was made in 1910 when *J. B. Herrick* examined an anaemic Negro student from the West Indies in Chicago. It was soon found that this condition was inherited, and that it was determined by a single dominant gene. Homozygotes suffered from sickle-cell disease, but heterozygotes were considered to be symptom free. This latter conception is no longer held. Double heterozygotes for the sickle-cell gene and either for the thalassaemia or for the haemoglobin C or the haemoglobin D gene may all suffer from a modified sickle-cell-anaemia. There is evidence that even simple sickle-cell heterozygotes may occasionally suffer from haemolytic crises, and that they have a high incidence of hyposthenuria. The sickle-cell crisis is thought to be due to intravascular sickling which causes both infarcts and haemolysis. The phenomenon is due to the low solubility of reduced haemoglobin S. *Pauling* and his associates were the first to describe the existence of this variant. In 1949 they sparated by electrophoresis haemoglobin S from haemoglobin A. They discovered that sickle-cell homozygotes did not possess haemoglobin A at all but that their red cells contained only haemoglobin S (and some small admixture of haemoglobin F). Sickle-cell heterozygotes possessed both haemoglobin A and haemoglobin S (fig. 1).

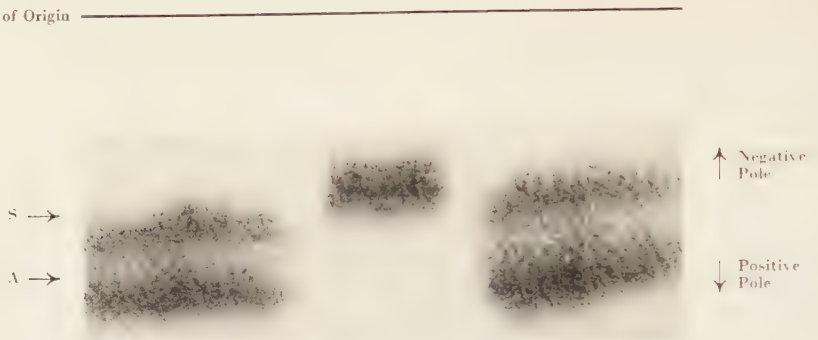


Fig. 1. Paper Electrophoresis at pH 8.6 of the Haemoglobins of a Nigerian Child and its Parents. The Parents possess Haemoglobins A and S. The Child is homozygous for Haemoglobin S; it was a Sickle-Cell Anaemia Patient under the Care of Dr. *J. H. Walters*, Yaba, Nigeria

Since then electrophoresis has been widely used to diagnose the sickling condition, and the technique has been responsible for the discovery of the other variants of haemoglobin A. Up to *Pauling*'s fundamental observation sickling had to be demonstrated *in vitro* by reducing a blood sample, and only rarely were sickle-cells seen on direct examination of blood smears or of histological specimens. A drop of blood is either incubated without access of air, in which case it will become de-oxygenated by the metabolic activity of the leucocytes, or reducing agents are added. In either case owing to its low solubility the reduced haemoglobin S will form an insoluble gel consisting of tactoids. These intracellular tactoids are responsible for the bizarre shape of the sickle-cell (fig. 2). The more rapid or the more profound the gel formation the more nearly the cells resemble a crescent moon or a sickle, intermediate forms are called oat-cells, and it is sometimes difficult for the less experienced to separate the intermediate shape from ordinary crenation.

By the application of the electrophoretic technique haemoglobins C, D, E, G, H, I, J, and K have by now been discovered (table 1). The letter B has not been allotted; it was originally given to to the sickle-cell haemoglobin, but was later replaced by the letter S for reasons of alliteration. If the methaemoglobin of *Hörlein* and *Weber* should turn out to be a haemoglobin variant as well it will be named haemoglobin M.

Most haemoglobins can be recognised by electrophoresis of a blood sample at alkaline pH (fig. 3). There is some difficulty in differentiating at alkaline pH between haemoglobins C and E, and between haemoglobins H, I, and J, K respectively, and further examination at acid pH

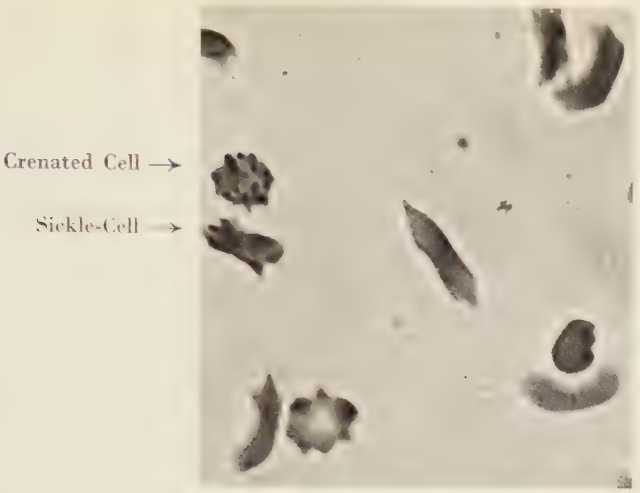


Fig. 2. A Sickle-Cell Preparation (× 1500).

may be necessary. Haemoglobins S and D have identical electrophoretic properties and cannot be told apart by this technique at all. However reduced haemoglobin D is not as insoluble as reduced haemoglobin S, hence it does not cause sickling *in vitro*. and solubility measurements will distinguish between the two.

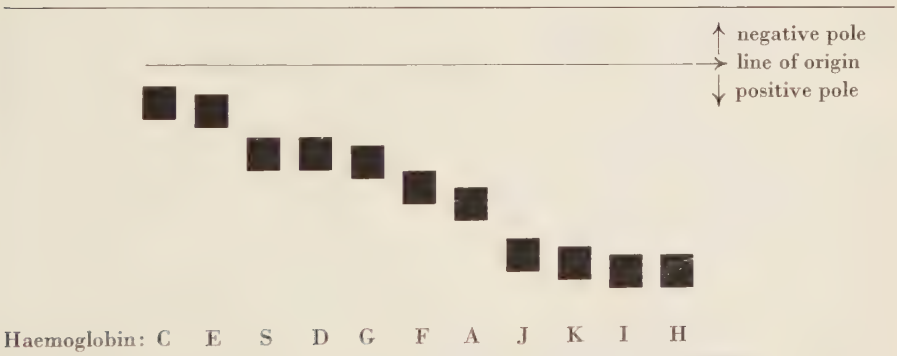


Fig. 3. Relative Position of Haemoglobin Variants in Paper-Electrophoresis at pH 8.6.

Recognition of genotype

Determination of the haemoglobin composition of a person's blood will usually not only determine the phenotype but the genotype also. There are however limitations to this seemingly easy way of establishing

Table 1. Known haemoglobin combinations. Thalassaemia is under a different genetical control from that of haemoglobins A, S, C and F and probably also from that of the other haemoglobins. Haemoglobin F is also under a different genetical control from that of haemoglobin A.

AA			Normal Adults
AA	F		Infants
AA	*T* F	(not always present)	Thalassaemia minor
AA	*TT* F	(nearly always present)	Thalassaemia major
SS	F	(nearly always present)	Sickle-Cell Anaemia
AS			Sickle-Cell Trait
AS	*T* F	(A not always found)	Microdrepanocytic Disease (Sickle-Cell: Thalassaemia)
CC	F	(sometimes present)	Haemoglobin C Disease
AC			Haemoglobin C Trait
AC	*T* F	(A not always found)	Haemoglobin C: Thalassaemia
SC	F	(nearly always present)	Sickle-Cell: Haemoglobin C Disease
DD			Haemoglobin D Disease
AD			Haemoglobin D Trait
(A)D	*T* F	(no A found; one case)	Haemoglobin D: Thalassaemia
SD	F		Sickle-Cell- Haemoglobin D Disease
EE	F	(traces occasionally)	Haemoglobin E Disease
AE			Haemoglobin E Trait
(A)E	*T* F	(20–40 % F, no A found)	Haemoglobin E: Thalassaemia
AA E			Traces of an E like Hb (A_2) can be found sometimes in normal individuals.
AA E	*T* F		Thalassaemia minor (*Kunkel-Wallenius* phenomenon) A_2 up to 15 %
GG		No anaemia	Homozygous G
AG			Haemoglobin G Trait
AH	*T*?	Genetical Position not yet clarified	Haemoglobin H Disease (Haemoglobin H: Thalassaemia?)
AI			Haemoglobin I Trait
AJ			Haemoglobin J Trait
AK			Haemoglobin K Trait

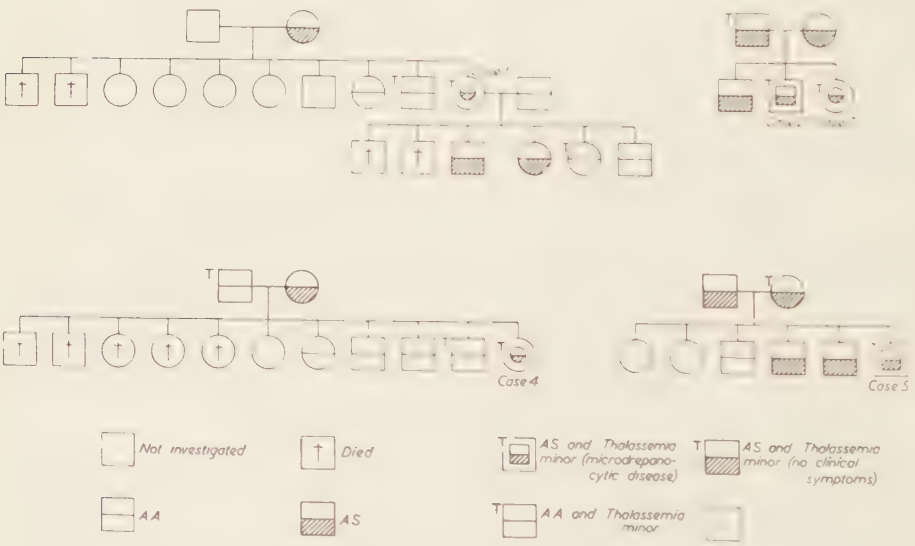
the haemoglobin genotype. So far only A, S and C have been proved to be allelomorphs. The finding of A + S, A + C, and S + C allows safe diagnosis of the respective genotypes. The same may be applicable to the finding of A + D, A + E and so forth. As regards E however it is important that it has been shown that normal adult haemoglobin consists of what we call haemoglobin A, and in addition of a small amount (normally not more than 3%) of a haemoglobin which has the electrophoretic properties of haemoglobin E. This fraction is so small that it is not usually recognised on simple paper electrophoresis. *Kunkel* and *Wallenius* have now shown that this haemoglobin E like compound (haemoglobin A_2) can be present at concentrations up to 15% in some thalassaemics. Thus the finding of a small amount of "E" in addition to haemoglobin A may not necessarily indicate that the person from whom the blood was obtained was an AE heterozygote.

The sole finding of haemoglobin A does not—at least in theory—allow the diagnosis of an AA genotype. It seems that the AH genotype gives normally rise to an AA phenotype. The inheritance of the H-haemoglobin has not yet been fully clarified. All AH phenotypes so far seen were double heterozygotes for haemoglobins A and H and for thalassaemia respectively. Where family studies have been possible it has always been found that both parents possessed haemoglobin A only, but that one of them was also a thalassaemia heterozygote. The available evidence suggests that H is absent in the phenotype of the genotype AH, unless there is also a suppression of A formation due to a thalassaemia gene, and that such double heterozygosity seems necessary for the penetrance of the gene responsible for haemoglobin H.

Of greater practical importance is that the finding of S or C or E only, does not establish a diagnosis of S or C or E homozygosity. A single thalassaemia gene can cause the complete suppression of haemoglobin A formation in the double heterozygote for the genes responsible for thalassaemia and for the haemoglobins A + S or A + C or A + E. In fact in the double heterozygote for thalassaemia and A + E (haemoglobin E : thalassaemia) A is regularly absent.

Few cases of haemoglobin C : thalassaemia have so far been observed, in some both haemoglobin A and haemoglobin C, in others only haemoglobin C were found. Sickle-cell : thalassaemia has been more widely studied. Haemoglobin A may either be absent, or be present in small amounts, or as far as haemoglobins A and S are concerned the laboratory findings may be indistinguishable from those seen in simple AS heterozygotes—though the additional presence of haemoglobin F may direct

the investigator towards the correct diagnosis. The clinical condition also shows a wide variation. Some patients have a severe sickle-cell anaemia, others show a modified sickle-cell anaemia, and yet others are clinically normal. To make matters more complicated: there is no strict correlation between the laboratory findings and clinical severity. In fact the interest of Dr. *Edington* and myself in sickle-cell : thalassaemia was first aroused by discovering in the course of a survey of Gold Coast Africans two adults who were not anaemic, but who as far as the composition of their haemoglobin was concerned differed in no way from homozygous sicklers. Clinical, laboratory and family studies are all required to determine whether a person is homozygous for the sickle-cell gene. Fig. 4 illustrates this point. It is taken from a study of sickle-cell : thalassaemia in Turkey by Dr. *M. Aksoy* and myself (Brit. med. J. in press). It will be noted that case 1 suffered from "sickle-cell anaemia" but was the parent of two non-sickling children. Examination of the haemoglobin in the laboratory showed that this woman was in fact suffering from sickle-cell thalassaemia, and that this explained why on marrying a normal husband she had two children with simple sickle-cell trait, one with thalassaemia minor, and one who was normal. Cases 2 and 3 and case 5 would on family study and on clinical observation alone be considered to be sickle-cell



FIVE PATIENTS WITH SICKLE CELL-THALASSEMIA DISEASE IN FOUR FAMILIES

Fig. 4

homozygotes. The laboratory tests revealed that one parent was a symptomless sickle-cell : thalassaemic, and that all three were in fact also heterozygous for thalassaemia and for the sickle-cell gene. Case 4 is an example of the contradictions which have been so frequent in the past before the laboratory was employed to complement family study and clinical diagnoses. This patient would have been considered a case of sickle-cell anaemia, and nonpaternity or mutation would have been suggested on discovering that the father was a non-sickler.

Population genetics

The life span of the AS cell is normal, but that of the SS cell is reduced, hence sickle-cell homozygotes suffer from a haemolytic anaemia. In addition, intravascular sickling will cause haemolytic crises, blockage of small vessels, thrombosis and infarcts. Haemoglobin variants other than S do not cause sickling, but homozygotes may show a reduced red cell survival. In the case of haemoglobin C disease (CC) this may cause a considerable haemolytic anaemia. In the others, increased red-cell destruction has not always been proved, and if it exists it seems to be well compensated by a greater activity of the bone marrow. However it is likely that additional stress may cause a haemolytic anaemia to become apparent. Thus homozygotes for the abnormal haemoglobin genes are at a disadvantage in the fight for survival. Sickle-cell anaemia especially removes homozygotes early in life before they have a chance to procreate. Yet the gene remains at high frequency in many parts of Africa, in some enclaves in Mediterranean countries, in the Middle East and India. Dr. *A. C. Allison* will discuss his noteworthy contributions to this problem. He has brought forward evidence that the sickle-cell trait affords protection against malaria. By a balanced polymorphism sickle-cell heterozygotes have a survival advantage over *both* normal and sickle-cell homozygotes, and the loss of sickling genes by the early death of sickle-cell homozygotes is compensated by a higher malarial death rate of normal homozygotes. Raper has continued *Allison*'s work in Uganda, and has fully vindicated *Allison*'s conclusions. He found that although there was no differential parasite rate when sicklers and non-sicklers were examined, there was in children at an age when acquired immunity had not yet been established, a difference in parasite density (*P. falciparum*). As death by malaria and severity of infection are related, this indicates a greater protection of sicklers.

Dr. *Raper* and I have recently examined an African tribe with a sickling incidence of 39% (Brit. med. J. in press). To our surprise we

Table 2. Balanced Polymorphism in an African Tribe.

Selection Acting First				
Population at Birth[1] (1000)	Selective Mortality		Undifferentiated Mortality	
	Malaria Deaths	Survivors (805, AS being 39%)	Deaths (AS = AA = 56.5%)	Survivors (350)
AS 314	0	314	177	137
AA 648	157	491	278	213

Selection Acting After Other Causes of Death				
Population at Birth[1] (1000)	Undifferentiated Mortality		Selective Mortality	
	Deaths (56.5%)	Survivors (419, 33% AS)	Malaria Deaths	Survivors (350, 39% AS)
AS 314	177	137	0	137
AA 648	366	282	69	213

[1] This includes 38 sickle-cell homozygotes (SS).
(From *Lehmann* and *Raper*, Brit. med. J. *2*, 333, 1956.)

found that the survival of sickle-cell homozygotes could not be considered to have any significant part in the maintenance of the high sickling rate (table 2). This meant that in every generation 19.5% of the sickling genes must be lost, and that a balance would therefore require an equivalent loss of normal haemoglobin genes from normal homozygotes only. It has been difficult to imagine how malaria could account for a loss of 24.2% of normal homozygotes.

This difficulty is however reduced if the overall death rate before puberty is taken into account. In this particular tribe a conservative estimate was about 65% mortality before the age of procreation. If sickle-cell anaemia and non-malarial undifferentiated mortality took their toll before malaria had to remove 24.2% of the normal homozygotes, the observable malarial death rate—though still 24.2% of normal homozygotes—would in fact only be 6.9% as far as all children born are concerned. Since malarial deaths are in fact likely to follow what must be a considerable proportion of the loss of child life—that in the first month or two—we may surmise that the observed figures would not be very much higher than the lowest possible figure of 6.9% of all children born.

These considerations bring to the fore the influence on the sickle-cell rate of the over-all infantile death rate. A primitive mode of life associated with a very high infantile death rate may be necessary to allow selective death by malaria to maintain very high sickling rates. In addition a low standard of life with high general morbidity will also expand malarial mortality itself and therefore increase the selective potentiality of this disease in a sickling population.

World distribution of abnormal haemoglobins and of thalassaemia

Haemoglobin S (fig. 5)

When sickling was first discovered in the United States it was soon noticed that the phenomenon seemed to be restricted to Negroes. Occasionally a "white" sickler was found, but almost always some Negro ancestry could be established eventually. It was not surprising therefore that sickling was found in a wide variety of African tribes. It was more noteworthy perhaps that there were considerable differences in incidence from tribe to tribe.

As far as the African continent is concerned sickling is virtually absent south of the River Zambesi. Elsewhere little is found whenever there is no malaria. But it is not possible to simplify and to assume that the incidence of sickling is merely determined by the effect malaria exerts on the proportionally higher survival rate of sickle-cell heterozygotes. In Uganda for instance there exist three major population groups: the Hamitomorphs, the Bantu and the Nilotes. The Hamitomorphs have as a rule only few sickle cells. They differ racially from the other Africans, and although deeply pigmented their features are europoid. They are cattle breeders, and forests and swamps are unsuitable for grazing their livestock. Thus in addition to their being racially distinct the Hamitomorphs live also in the least malarious regions. The Bantu tribes show varying sickling incidences. Those who have mixed mostly with the Hamitomorphs also live by virtue of that association in the least malarious parts of Uganda. The further a Bantu tribe is removed both geographically and racially from the Hamitomorphs, the higher is the sickling rate. An interesting community are the Teso who have a high sickling rate. They speak a hamitic language, and are therefore often grouped with the Hamitomorphs. If this is done the Teso will represent an exception to the rule that Hamitomorphs show no or only a few sickle-cells. Yet although the Teso are affiliated with the Hamitomorphs because of their language they are quite different from them physically. They are not cattle breeders and have moved into malarious country where they have intermarried with Bantus and Nilotes. Thus they differ from the Hamitomorphs both in their nasal index and in their ecology. The Nilotes of Uganda have all fairly high sickling incidences, excepting the Madi in the most northerly region of the Protectorate. The southern Sudanese Nilotes who are their neighbours also have no sickle-cells. Yet there is no appreciable difference in malarial epidemicity between the part of

Uganda where most of the Uganda Nilotes live, and the southern region of the Sudan.

Fig. 5. Distribution of Sickle-Cells.

The presence of sickling in some communities in Mediterranean countries and in the Middle East can partially be explained by the importation of African slaves in Roman times. In India so far only remote aboriginal tribes have been found to harbour the sickling trait, which is absent from the Dravidian and Aryan populations. It is unlikely that a contact with Africans can have been restricted to these few pre-Dravidian groups. Sickling could of course have arisen in India by independent mutation. It seems more likely to me that the gene has entered Africa and India from one and the same source which for many other common features has been the Middle East. In India the sickling tribes are at the present all Veddoids; although many non-Veddoid aboriginal groups have been examined no sickling has been found amongst them. Occasionally a sickler has been found in a non-Veddoid neighbouring tribe, and also not all Veddoid groups have been found to show sickling. It is thought that Veddoid races populated Arabia in the Neolithic period, and that

they were driven towards the South both into Africa and into India by climatic changes in this once green and fertile peninsula. Veddoid features have been noticed in prehistoric skeletons found in Mediterranean countries, and it may not be fantastic to assume that some of the sickle-cell genes in North Africa and in southern Europe, and perhaps even more so in Arabia are inherited from these older populations.

Haemoglobin C (fig. 6)

Fig. 6. Distribution of Haemoglobin C in Africa. ■ Incidence above 15 per cent. ⊞ Incidence 10–15 per cent. ||| Incidence 1–9 per cent. |||| single instances reported.

Haemoglobin C was discovered in a North American Negro family. As the American Negro came from West Africa it was to be expected that this haemoglobin should occur in that part of the world. It was however surprising that haemoglobin C which is not very frequent in the North American Negroes has a very high incidence in certain parts of west Africa. In the Northern Gold Coast haemoglobin C is more often found than sickling. Within the Gold Coast the frequency falls from North to South (table 3), and it falls still further towards the East and the West of that Colony. There is virtually no haemoglobin C in the Congo, in South Africa and in East Africa. Occasionally a person with that haemoglobin has been found in these parts, but this was explained by the importation

Table 3. Haemoglobin Variants in 466 Africans from the Gold Coast.

Area		AA	AS	AC	SC	CC	AG
Southern	No.	131	34	16	1	–	1
183	%	71.5	18.6	8.7	0.5	–	0.5
Northern	No.	205	17	57	2	2	–
283	%	72.4	6.0	20.1	0.7	0.7	–

Proportion of People with Abnormal Haemoglobins

Area	Abnormal haemoglobins per cent	S per cent	C per cent
Southern 183	28.4	19.1	9.8
Northern 283	27.6	6.7	21.5

(From *Edington* and *Lehmann*, Man, *56*, 34, 1956.)

of slaves from the West. The same explanation has been advanced for the finding of some people with haemoglobin C amongst Algerian Muslims and Berbers of Morocco. There is a considerable contrast between the distribution in Africa of haemoglobin S and haemoglobin C. The first is found all over tropical Africa from East to West South of the Sahara, the second is restricted to the West and shows a focus somewhere in the Gold Coast from where it seems to be spreading. It is tempting to speculate as Dr. *Mourant* has done that haemoglobin C has arisen as a mutant of haemoglobin S. The homozygous C condition is much less severe than sickle-cell anaemia. In contrast to sickling homozygotes quite a few haemoglobin C homozygotes are well known to survive into adult age and to have offspring. While the AC heterozygote may enjoy advantages similar to those which the sickle-cell trait confers, there would be in the homozygotes less loss of C genes before puberty than of S genes. We may thus be witnessing the spread of a new gene more advantageous than that for sickling, which might be destined to replace the older and less viable mutation. I like to quote from a letter by *J. V. Neel:* ". . . Never in the history of genetics, with the possible exception of *Ford*'s melanism story in the moth, have geneticists and those with kindred interests been quite so close to having a ringside seat at the origin and dissemination of a 'new' gene."

Haemoglobin G

Whereas haemoglobin S is spread all over the "sickle-cell belt" of Africa, and haemoglobin S though more restricted is covering a large area in the west of the continent, we have in haemoglobin G a variant which up to recently had been found in only one family. It was discovered by chance during a survey of Gold Coast Africans. The father of the family belongs to the Ga tribe and lives near Accra. He turned out to be a homozygote, and it seemed likely that haemoglobin G should turn up again on further search, but although many thousand West Africans and many hundred Ga amongst them have been examined since, no further instance of G has been found. However recently G has been discovered by Dr. *Rose Schneider* in a Negro family in Texas.

Haemoglobin D (fig. 7)

Haemoglobin D has up to recently been considered rare. It was first seen in a American "white" family, and later on instances were reported from Britain and from North Africa. However when North-West Indians (Sikhs and Punjabi Hindus) were examined haemoglobin D turned out to be present at a frequency of 2 %. Gujeratis who are derived from further south in West India show a frequency of 1 %. One case was dis-

Fig. 7. Haemoglobin D ≡ and E ◆.

covered amongst 400 Turks, and recently a Persian girl has been seen in London whose mild anaemia seemed to be due to haemoglobin D : thalassaemia.

Haemoglobin E (fig. 7)

Although haemoglobin E was discovered in a part East Indian child this variant has not been found again in Indians until very recently when a few examples were seen in Bengalis. It is present in frequencies of over 10 % in Siam, Burma and North-Eastern Malaya. From there the incidence falls towards the South, and is about 2 % in Indonesia. It is present at a similarly low incidence in the Veddas of Ceylon, but not in the Singhalese themselves, and in the Dayaks of Sarawak. No haemoglobin E has been found among Chinese although a number of investigators have made extensive surveys.

Haemoglobin H

We know at present only of a few instances of haemoglobin H. No doubt the fact that H will appear in the phenotype of the AH genotype only when there is also thalassaemia present (see above) will make it rather difficult to determine the true incidence of this haemoglobin variant. Of the few observations which have been made most were obtained in Chinese, Philippinos, and one was made in Malaya. However haemoglobin H has also been seen in a Greek family and in a Transjordanian Arab.

Haemoglobins I, J, and K

Haemoglobins I and J were again first seen in North American Negroes. More cases of J have been reported from Liberia and some have been seen among Algerian Muslims. Haemoglobin K has been found in Liberia and in the Kabyles of North Africa.

Thalassaemia

Thalassaemia or Mediterranean Anaemia was first so called because of the frequency at which the condition was noted in Greeks and Italians. It has become increasingly clear that thalassaemia is by no means restricted to the Mediterranean races. It is perhaps the most widely distri-

Fig. 8. Distribution of Thalassaemia.

buted haemoglobinopathy, its incidence ranging in the Old World from Western Europe and West Africa in the West to China and the Philippines in the East. So far thalassaemia has not been found widely distributed in Africa, and even in West Africa there are only few well proven instances.

Allison, A. C.: Acta genet. *6*, 430–434, 1956/57

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POPULATION GENETICS OF ABNORMAL HUMAN HAEMOGLOBINS

By A.C. ALLISON

Ten genetically controlled abnormal haemoglobin types have now been characterized (haemoglobins S, C, D, E, G, H, I, J, K and M). Their properties have recently been summarized by *Zuelzer*, *Neel* and *Robinson* [1956]. The genes for haemoglobins G, H, I, J, K and M seem to be rather uncommon in most populations, so that they can properly be regarded as mutants which are kept at a low frequency by the operation of selection against them; this occurs when any two abnormal haemoglobin genes come together in the same individual and thereby produce an anaemia.

On the other hand, the genes for haemoglobins S, C and E, and the thalassaemia gene, have attained high frequencies in many human populations despite the fact that selection operates against homozygotes and against those who carry two different abnormal haemoglobin genes. These characters are undoubtedly polymorphic. The case of haemoglobin D, which seems to be present in about 2 per cent of Sikhs and to produce a homozygote with polycythaemia as the only detectable abnormality (*Bird* and *Lehmann* [1956]) is marginal, but probably represents a true polymorphism.

An adequate explanation for the polymorphism of the sickle-cell character in East Africa is available. Electrophoretic analyses performed in 729 African infants show the proportion of sickle-cell homozygotes expected from the *Hardy-Weinberg* law, which confirms that there is no significant selection against sickle-cell homozygotes *in utero*. Similar analyses carried out on 6840 adult Africans show that on both the East and West sides of the continent the proportion of sickle-cell homozygotes surviving to adult life is less than 20 per cent of the average survival of all genotypes (*Allison* [1956b]). This order of survival is confirmed by

clinical studies. The sickle-cell heterozygote seems to have a considerable advantage—up to 25 per cent—over other genotypes. The advantage can be attributed mainly to resistance against *falciparum* malaria, although other factors (e.g. resistance to hookworm infestation—*Raper* [1956] may play a subsidiary part. It can now be taken as established that children who are heterozygous for the sickle-cell gene have lower malaria parasite counts than other children. Since the mortality from *falciparum* malaria is known to be related to the height of the parasite count (*Field* [1949]), it seems reasonable to conclude that the mortality from malaria will be lower in sickle-cell heterozygotes than in other genotypes. And there is direct evidence that the heterozygotes rarely, if ever, develop potentially fatal complications of malaria, such as cerebral malaria and blackwater fever (*Raper*, loc. cit.). The advantage of the heterozygote appears also in their significantly higher incidence in adult than in infant African populations (*Allison* [1956b]). The distribution of the sickle-cell gene is also in accordance with this hypothesis: in Africa and elsewhere high frequencies are attained only in malarious regions. Thus, the equilibrium of the sickle-cell gene and its normal allelomorph in East Africa seems to be stable, with the sickle-cell heterozygote at an advantage and the homozygote sub-lethal.

In West Africa the position is complicated by the presence of a third allelomorph, the haemoglobin C gene. A year ago, when the position was reviewed by *Allison* [1956a], the only information available was that the haemoglobin C gene was present at a frequency of about 5 per cent in the Southern Gold Coast and had not been found in East Africa. Since it was known that persons who inherit the sickle-cell gene from one parent and the haemoglobin C gene from the other sometimes develop a condition very like sickle-cell disease (see, e.g. *Smith* and *Conley* [1954]), *Allison* postulated that the sickle-cell and haemoglobin C genes must tend to be mutually exclusive in human populations. Extensive data published since then (*Edington* and *Lehmann* [1956], *Allison* [1956b]) have provided a fair overall picture of the distribution of the sickle-cell and haemoglobin C genes in West Africa and have confirmed *Allison*'s postulate. The frequency of the haemoglobin C gene rises to 13.5 per cent in the Dagomba tribe of the Northern Territories of the Gold Coast; in this tribe the frequency of the sickle-cell gene is only 2 per cent. On all sides of this main focus the populations tested have shown a cline of descending frequencies of the haemoglobin C gene and increasing frequencies of the sickle-cell gene. The negative correlation between the frequencies of the two abnormal genes appears in fig. 1.

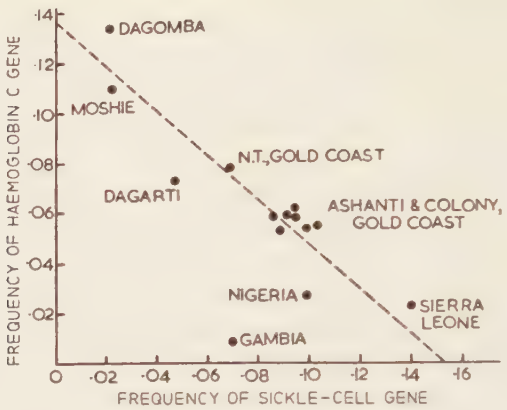

Fig. 1

Allison [1956b] has also made a preliminary calculation of the fitnesses of the various genotypes on the basis of electrophoretic tests of haemoglobin specimens in 1042 adult Africans from the Gold Coast. The reduced viability of sickle-cell and haemoglobin C homozygotes and the sickle-cell: haemoglobin C heterozygote is reflected in the relatively low frequency of persons with these genotypes in the adult population. Equating viability between birth and reproductive age with fitness, the following estimates of fitness were obtained (symbols of *Allison* [1955]):—

$Hb^A/Hb^S = 1.138$	$Hb^C/Hb^C = 0.550$
$Hb^A/Hb^C = 1.103$	$Hb^S/Hb^C = 0.407$
$Hb^A/Hb^A = 0.976$	$Hb^S/Hb^S = 0.192$

All homozygotes are at a disadvantage, the normal less than the abnormal; the Hb^S/Hb^C heterozygote is also at a disadvantage, but the other heterozygotes are favoured.

The conditions required for genetic equilibrium of three allelomorphs have been analysed by *Owen* [1953] and by *Penrose, Smith* and *Sprott* [1956]. The latter have shown that with the fitness values quoted above the equilibrium is stable but only by quite a small margin. It is uncertain whether Hb^S and Hb^C would, in fact, return to the same proportion if there were a chance variation. By slightly altering the fitness values, a semi-stable equilibrium is obtained, in which, if the frequencies are disturbed from the equilibrium values within a definable subspace, they will remain at their new values. If they are moved outside the subspace, they will be restored by selection to some point within the subspace, not necessarily the original point.

In this instance the equations determining the subspace lead to a single equation $162a_2 + 127a_3 = 24$, where a_2 is the frequency of Hb^S

and a_3 is the frequency of Hb^C. It is therefore interesting to see whether the values of Hb^S and Hb^C observed in different West African populations fit this equation. The data so far published are given in table 1.

Table 1

Population	Number tested	Hb^S	Hb^C	$162a_2+127a_3$	Observer
Dagomba, N. Gold Coast	71	0.021	0.134	20.42	1
Moshie, N. Gold Coast	115	0.022	0.105	16.95	1
Dagarti, N. Gold Coast	97	0.047	0.072	16.76	1
Miscellaneous, N. Gold Coast	275	0.069	0.078	21.09	2
Zabrama, Togoland	63	0.103	0.048	22.79	2
Ashanti, Gold Coast	102	0.108	0.044	23.09	2
Ga, S. Gold Coast	174	0.098	0.043	21.34	2
Fanti, S. Gold Coast	156	0.103	0.052	23.29	2
Ewe, S. Gold Coast	167	0.112	0.045	23.85	2
Twi, S. Gold Coast	104	0.101	0.048	22.46	2
Miscellaneous, S. Gold Coast	283	0.096	0.049	21.74	1
Miscellaneous, Nigeria	247	0.109	0.027	21.18	2
Miscellaneous, Sierra Leone	218	0.140	0.023	25.60	2
Miscellaneous, Gambia	1442	0.070	0.009	12.48	2

Observers: (1) *Edington* and *Lehmann* [1956]; (2) *Allison* [1956b].

In view of the relatively small number of individuals on which the gene frequency and fitness estimates are based, the values of $162a_2+127a_3$ are in fair agreement with expectation in all populations except the Gambians. Most of the observed values are somewhat below 24, which suggests that the estimates of fitness may not be quite correct. The Gambia seems to be a marginal region with a very heterogeneous population in which the frequencies of the abnormal haemoglobin genes may not yet have been stabilized by selection (*Allison* [1956b]). On the whole, these results suggest that the other West African populations tested have lived long enough in relatively uniform environments to show frequencies of the abnormal haemoglobin genes close to those predicted for a semi-stable equilibrium from the estimated fitnesses of the several genotypes.

With such a system, there is only a small probability that the haemoglobin C gene could have attained the high frequencies now observed if it had arisen by mutation in a population already having a high frequency of the sickle-cell gene. The most likely inference is that the haemoglobin C gene has been favoured in some population in or near the Northern Gold Coast having a low frequency of the sickle-cell gene. The haemo-

globin C gene diffused out of this area into populations with higher frequencies of the sickle-cell gene, and through selection the frequencies of the two abnormal genes have been brought to various points close to the subspace for a semi-stable equilibrium as defined above.

The population genetics of haemoglobin E and thalassaemia in South-East Asia and the Mediterranean countries have not been worked out, but it seems likely that the situation will turn out to be quite similar to that obtaining in the case of the sickle-cell and haemoglobin C genes in Africa.

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Discussion:

J. V. Neel (Ann Arbor, Michigan): Dr. *Lehmann* and Dr. *Allison* have presented in a beautifully clear fashion certain aspects of the problems associated with the abnormal hemoglobins. It is a comment on the swift progress of the field of human genetics that until 8 years ago we did not even recognize the existence of abnormal hemoglobins.

First of all I should like to endorse Dr. *Lehmann*'s plea for an elastic terminology. My collaborators and I have evidence that gene responsible for hemoglobin C_1 is not an allele of the gene responsible for hemoglobin S. The Thalassæmia locus seems separate from both of these, while there are theoretical reasons for postulating that the production of hemoglobin F depends upon activity at still another locus. This is going to be a situation of some genetic complexity, where the need for an adjustable and descriptive terminology is great.

Secondly I would mention the recent finding of my collaborators and myself that hemoglobin J otherwise known on the basis of a single family, occurs in approximately 1 % of Liberians. It is tempting to speculate from the known distributions of hemoglobins J, C and S that here are three successive stages in the process whereby a "new" human gene becomes established and disseminated.

Finally, with respect to the "malaria hypothesis", as I pointed out last year in the Galton lecture, the hypothesis demands a higher death rate from malaria than many malariologists would accept. If the malaria hypothesis becomes firmly established, and results in a reappraisal of malaria deaths, here is a new example of the uses of the genetic approach. I would hope that in accepting the malaria hypothesis we not abandon the search for other factors of importance in maintaining this polymorphism, since here we have a situation which will be widely quoted, and the need to be critical is great.

Gartler, S.M., I. L. Firschein and *T. Gidaspow:* Acta genet. *6*, 435–446, 1956/57

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SOME GENETICAL AND ANTHROPOLOGICAL CONSIDERATIONS OF URINARY β-AMINOISOBUTYRIC ACID EXCRETION

By STANLEY M. GARTLER, I.L. FIRSCHEIN and T. GIDASPOW

Introduction

β-aminoisobutyric acid (BAIB) was first detected in human urine by *Crumpler, Dent, Harris* and *Westall* [1951] and independently by *Fink* [1951]. It was observed that this non-protein amino acid was excreted in urine in widely varying concentrations from person to person, but at a relatively constant rate for any one individual. Certain genetic possibilities were immediately apparent and *Harris* [1953] went on to explore them with success. At the same time the work of *Fink* [1951] and *Fink, Henderson* and *Fink* [1951] revealed that the excretion rate of BAIB could be related to certain disease processes which together with the genetical facts derived by *Harris* made a most interesting picture. At this stage it was clear to us that an extensive study of urinary BAIB excretion would fit exceedingly well into our program of the investigation of the role of physiological variation in human evolution.

In this respect we might comment briefly on our approach to the question of the role of physiological variation in human evolution. Three general problems present themselves in this respect: (1) the extent and nature of hereditary control over the physiological variables in question, (2) comparative data on man and the anthropoid apes and of various human populations with regard to the character, and (3) the adaptive significance of the physiological variable. It is within this conceptual framework that we have approached the study of BAIB excretion, the hope being that when sufficient data in the three areas mentioned are

accumulated, that a meaningful interpretation of the evolutionary role of BAIB excretion can be obtained. Today we are still a good distance from our goal and so we can bring you only a skimming of facts and the most tentative of conclusions.

Genetic Control of BAIB Excretion

The first genetic study of urinary BAIB excretion was carried out by *Harris* in England in 1953. Using paper chromatographic techniques, *Harris* classified individuals as either high or low excretors of BAIB depending on the intensity of the BAIB spot on the urine chromatogram relative to other amino acids, especially alanine. When the BAIB spot was of equal or greater intensity than that of the alanine spot on the same chromatogram the individual was classified as a high excretor. On the basis of this simple dimorphism between high and low excretors, *Harris*'s family data were in good agreement with the hypothesis that a single gene difference underlies the observed variability (high excretors being homozygous for a single recessive gene and low excretors being either homozygous or heterozygous for the dominant allele). A second family study of BAIB excretion, using similar methods of classification, was carried out in Italy by *Calchi-Novati*, *Ceppellini*, *Biancho*, *Silvestroni*, and *Harris* [1954] and its results were also in agreement with a simple one gene hypothesis.

No gross effects of diet on BAIB excretion were observed in these studies nor was any difference in the frequency of high excretors among the sexes observed. Our observations are in general agreement with these conclusions. However, a markedly increased frequency of high excretors was observed among children under five years of age in the second study and this observation has been confirmed in the work of *Gartler* and *Kraus* [1956]. Dr. *Ceppellini* has suggested in a personal communication that this increased frequency among the very young may represent the expression of the heterozygote which is masked in later life. From the standpoint of population genetics the data of *Gartler* and *Kraus* [1956], shown in table 1, support this idea. However, they are very limited, and without family studies such data would not be adequate for a demonstration of this hypothesis.

Though these studies formed a very agreeable picture of the genetics of BAIB excretion, it appeared from other data (*Berry* [1953]) that the real nature of the distribution of the urinary excretion of BAIB might be continuous and not dimorphic as assumed in the above genetic studies.

Table 1. Distribution of high excretors[1] under and over 5 years of age among Apache Indians, and its possible significance to change of dominance relationship with age.

Age	Total no.	% high excretors	Gene frequency[2] T	Gene frequency[2] t	Expected %[3] of high excretors under 5 if high excretion dominant
< 5	14	85.7			87.2
$\geqq 5$	113	41.2	.36	.64	

[1] Optical density BAIB/optical density alanine $\geqq 1.0$.
[2] t (recessive allele for high excretion) $= \sqrt{\text{freq. high excretors} > 5}$
[3] $t^2 + 2Tt$

This raised the possibility that the genetic picture might be more complicated than indicated, and therefore it was felt worthwhile to undertake a more quantitative family study of BAIB excretion (*Gartler* [1956]). Urinary BAIB was measured by paper chromatographic techniques and the concentration expressed as mg BAIB/mg creatinine in the urine. The data clearly showed that the distribution of BAIB excretion was continuous and not dimorphic. Furthermore, there was no evidence of bimodality in the population investigated, which made the testing of any simple genetic hypothesis somewhat arbitrary. However, since it was felt that the absence of bimodality was largely due to the relatively small size of the sample (according to *Harris*'s classification less than 15 individuals in the sample of 282 would be classed as high excretors), a dividing line was drawn between high and low excretors at .030 mg BAIB mg creatinine, and the data tested for agreement with a simple one gene hypothesis (high excretors homozygous recessive). The dividing line was drawn at this point since for several reasons it was considered to be the minimal level for a high excretor. The agreement with hypothesis was excellent and lent considerable support to *Harris*'s original view.

However, we do not feel that this closes the genetic chapter on BAIB excretion. Certainly, a bimodal distribution must be demonstrated and as yet, the distributions obtained from studies of populations with a high frequency of high excretors have not been too convincing. On fig. 1 are shown two such populations, the data being expressed as a ratio of the optical densities of BAIB/alanine. This method, which is essentially *Harris*'s, of expressing the data has at least two advantages. (1) It corrects for the effect of a generalized aminoaciduria, which may be important not only in assaying differences between individuals but also in comparing different populations. As an example we may note the comparison of ranges for BAIB excretion for three populations (N.Y.C. whites, Apach Indians and British Honduras Caribs) when the data are expressed as mg BAIB/mg creatinine and as optical density BAIB/optical

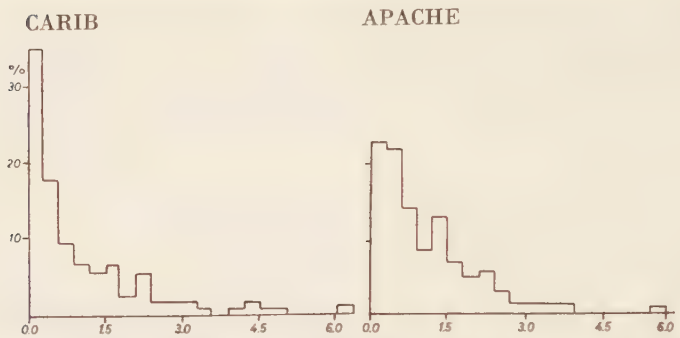

Fig. 1. Frequency distributions of the urinary excretion rate of BAIB in two populations.

density alanine. The Apache Indian population has a most interesting general aminoaciduria (the average BAIB concentration alone is 0.080 mg BAIB/mg creatinine), and as can be seen in table 2, when the data are expressed as ratios of optical densities, its BAIB excretion range is quite comparable with those of the other populations. A second reason for the BAIB/alanine method of expressing the data is that it is becoming increasingly apparent as has been so well demonstrated for cystinuria (see *Harris* [1953a], for general discussion), that it is the pattern of amino acid excretion rather than the excretion rate of the individual amino acid which is likely to be of most genetic interest. The work of *Pare* and *Sandler* [1954] on march hemoglobinuria is particularly convincing in this case. In march hemoglobinuria a renal tubular reabsorption defect for hemoglobin is present, which *Pare* and *Sandler* found to also lead to amino aciduria for cystine and BAIB. The β-aminoisobutyric aciduria in these cases is definitely distinct from the general hereditary type we have been discussing and yet it could only be distinguished by pattern analysis. Furthermore, these cases bring up the point that the BAIB/alanine ratio may not be the best way of expressing BAIB excretion for genetic purposes, since it would not separate out the admittedly rare march hemoglobinuria cases.

Let us return to the population distribution shown in fig. 1. While there are indications of bimodality, and even trimodality, in these distributions, they certainly cannot be considered as conclusive. There are a number of potential reasons for the lack of a distinct bimodal distribution (sample size, complicating genetic factors, method of expressing data, environmental effects, or any combination of these). However, there are not sufficient data at present to warrant detailed consideration of any of them. Suffice it to say that the family studies to date have not been of

Table 2. Comparison of ranges of *BAIB* excretion for three populations with data expressed as mg *BAIB*/mg creatinine and as the optical density *BAIB*/optical density alanine.

	N.Y.C. Whites	Apache Indians	British Honduras Caribs
mg *BAIB*/mg creatinine . . .	0.010–0.110	0.010–0.450	0.010–0.110
optical density *BAIB* optical density alanine	0.1–4.8	0.1–6.0	0.1–7.0

sufficient size (in terms of the number of segregating families observed) to exclude alternative, but more complicated genetic hypotheses such as one of multiple alleles. In this respect we should like to point out, that for further elucidation of the genetic basis of BAIB excretion, it is desirable to carry out family studies in populations with a high frequency of high excretors. White populations are definitely not satisfactory in this respect, but other groups, with high excretion rates have been found, and it is to be hoped that family studies in these groups will be carried out.

Comparative data on BAIB excretion for man and the Anthropoid Apes and for various racial groups

In the course of a study on urinary amino acids in the great apes (*Gartler, Firschein* and *Dobzhansky* [1956]) we were able to collect comparative data on BAIB excretion for the animals investigated. Since that time we have enlarged the series somewhat and the combined data are given in table 3. None of the 55 animals studied was classified as a high excretor of BAIB. These results cannot be considered as final for the lower primates, but they certainly are indicative and suggest to us the possibility that the genetic control of high excretion of BAIB may represent a relatively recent hereditary change in human evolution. Further work on this phase of BAIB excretion is highly desirable; we hope to extend the above series to include more subjects, and when the opportunity permits, to carry out critical physiological experiments on the metabolism of BAIB in these primates.

Our main effort at the present time has been a comparative study of BAIB excretion among various human populations. To this date, three studies of at least 100 individuals each have been carried out in this laboratory. They include N.Y.C. whites, British Honduras Caribs Negroes, and Apache Indians of Arizona. The results of these studies are given in table 4, the BAIB concentration being expressed as a ratio of optical densities (BAIB/alanine), and the data have been broken down into three categories: < 1.0, 1.0–2.0, and > 2.0. The only disturbing item in the

Table 3. Results of testing for excretion of Urinary BAIB among various Primates

Species	No.	Sex	BAIB Excretors High Excretors	BAIB Excretors Low Excretors
Chimpanzee .	15	♂	0	15
	22	♀	0	22
Gorilla . . .	5	♂	0	5
	3	♀	0	3
Orang . . .	2	♂	0	2
	1	♀	0	1
Gibbon . . .	1	♂	0	2
	1	♀	0	1
Macaca . . .	3	♂	0	3
Cebus	1	♂	0	1
Papio . . .	1	♂	0	1
Totals . . .	55		0	55

table is the sex difference in the Apache Indians for the category > 2.0 (difference significant at the 5 percent level). However, this difference may not have any adverse effect upon the genetic scheme, since there is no sex difference in the Apaches if we pool the classes above 1.0. This is, of course, what has been done in the genetic studies thus far.

Table 4. BAIB Excretion expressed as optical density BAIB optical density alanine in Whites, Caribs and Apache Indians.

		% < 1.0	% (1.0–2.0)	% > 2.0
N.Y.C. Whites N = 218 . .	♂	0.942	0.048	0.010
	♀	0.942	0.058	0.000
	Combined	0.942	0.053	0.005
British Honduras Caribs N = 285	♂	0.672	0.198	0.130
	♀	0.696	0.162	0.142
	Combined	0.684	0.180	0.136
Apache Indians N = 113 . .	♂	0.582	0.218	0.200
	♀	0.586	0.345	0.069
	Combined	0.584	0.283	0.133

As can be seen in table 4, the range of variation of the frequency of high excretion among the populations studied is considerable (assuming a value of 1.0 or greater as a high excretor, the range extends from 6 % in whites to over 40 % in Indians). Major investigations by other laboratories have included only white populations e.g. English (*Harris* [1953]) Italians (*Calchi-Novati* et al. [1954]). All of these have yielded frequencies

of high excretors in the range from 5 to 9 percent. The results of these studies are quite similar and definitely establish that the frequency of high excretors in whites of western European descent is relatively low, being less than 10 %. The high frequency found in the Apache Indians is particularly interesting in view of the reports of high frequencies of high excretors among Japanese and Chinese (*Ishihara* and *Komori* [1952]: 24 % high excretors among 17 Japanese; *Sutton* and *Clark* [1955]: 28 % high excretors among 19 Chinese).

The Carib data may turn out to be extremely interesting in regard to analyzing the migrational history of the Carib people and one of the authors (I. L. F.) is at present engaged in such a project. At the present time, the only comparative data we have for the Caribs consists of a small sample (38) of New York City Negroes, all male, and selected on an anthropological scale for extreme negroid features. The frequency of high excretors in this sample was 15 percent. Another interesting comparative group in this respect consists of 30 Caribs residing in New York City. The frequency of high excretors in this study was 23 percent. While this lower value for the New York City Caribs is not significantly different from the British Honduras value, we are concerned about it and are attempting to increase our sample of local Caribs.

It seems clear to us from these beginning investigations that the extension of comparative studies of BAIB excretions will be of considerable value in the genetical-anthropological area. We hope to continue our work along this line combining it with family studies whenever possible. At the same time we are attempting to attack the question of the adaptive significance of β-aminoisobutyric aciduria, and we will now consider this aspect of the problem.

Adaptive Considerations of BAIB Excretion

We may consider first the question of the physiological basis of β-aminoisobutyric aciduria. *Fink* and her colleagues [1951, 1956, and 1956] have attacked the problem of the metabolic source of BAIB. Working in vivo and vitro with the rat, they have amassed considerable evidence in favor of their view that BAIB is a product of nucleic acid catabolism. More specifically, they consider it to be derived from pyrimidine catabolism by the following scheme:

thymine ← dihidrothymine ⇌ β-ureidoisobutyric acid → BAIB.

If this is so, and there appears to be no evidence to the contrary, then we are certainly dealing with a potentially very important physiological process.

The next question is whether a difference in the rate of nucleic acid catabolism is the basis of the difference between high and low excretors of BAIB. The evidence at present appears to be to the contrary. Rather it seems that a specific difference in the kidney tubular reabsorption mechanism for this amino acid is responsible. This hypothesis was originally suggested by *Crumpler*, *Dent*, *Harris* and *Westall* [1951] and was based on paper chromatographic studies of plasma amino acids which revealed no difference between high and low excretors of BAIB with respect to plasma BAIB concentration. However, actual plasma levels of BAIB were not reported by these workers, presumably because of the difficulty in quantifying by paper chromatographic techniques substances in such low concentration as plasma BAIB must be. Recently, *Evered* [1956], using ion exchange methods reported actual plasma concentrations of BAIB for one high and two low excretors. He also reported the 24 hour urinary output of BAIB for these individuals, and the combined results are in agreement with the view that in high excretors, BAIB is filtered freely through the kidney into the urine, while in low excretors, BAIB is reabsorbed by the kidney tubules from the glomerular filtrate with a high degree of efficiency. This work then strongly supports the kidney reabsorption hypothesis, although it certainly must be extended to cover more individuals before it can be considered as conclusive. Furthermore, the reabsorption hypothesis, even if proven correct, does not entirely explain the physiological basis of BAIB excretion. For even if we assume a difference in renal thresholds as the basis of the observed difference of the BAIB excretion of high and low excretors, then we are faced with the most interesting question of what the low excretors do with their BAIB or some precursor of it? Then too, there are certain observations which at present tend to cloud this story, though when fully explained will surely be most illuminating.

These observations are concerned with the relationship of BAIB excretions to various pathological conditions and they bring us to that phase of the problem which we might entitle "adaptive studies of BAIB excretion." We use the term adaptive at this point in a strictly genetical sense, that is, with regard to possible differential reproductive values for high and low excretors. A direct approach to this problem would require differential studies of fertility and mortality and as yet such work has not been undertaken.

A more indirect, but clearly important, approach to the problem of genetic adaptiveness is that of the investigation of possible relationships between alternative phenotypes and various diseases. The current blood

group work along this line will probably become a classic example of this approach. With regard to BAIB excretion there are a number of reports indicating that in various pathologies the level of BAIB excretion is significantly above normal (malignancies, tuberculosis, march hemoglobinuria and havy-metals poisoning; *Fink*, *Henderson* and *Fink* [1951], *Clarkson* and *Kench* [1956], *Ishihara*, *Komori* and *Yokoo* [1953], *Ishihara* and *Komori* [1952], *Gartler* and *Werthamer* [1956], *Pare* and *Sandler* [1954]). It is obvious that not all of these reports represent hereditarily determined high excretors of BAIB in the sense that we have been discussing them up to now. The heavy-metals poisoning cases most likely represent externally-induced kidney lesions. In march hemoglobinuria we are evidently dealing with a non-specific renal tubule reabsorption defect involving hemoglobin, cystine, and BAIB. Since cystine excretion is not generally correlated with BAIB excretion, it seems that this anomaly represents an independent pathway leading to elevated BAIB excretion. It would be most interesting to know what genetic implications, if any, there are in march hemoglobinuria. In pulmonary tuberculosis, the β-aminoisobutyric aciduria is evidently part of a generalized aminoaciduria due to the wasting process of the disease. In the malignancies, a generalized aminoaciduria may also account for some of the cases of elevated BAIB excretion, but in many instances, the increase of BAIB excretion is relative to other amino acids, and these cases must be considered as significant. Whether or not these cases represent hereditarily determined high excretors of BAIB, who for some reason are more prone to malignancies is an unanswered and important question.

Let us consider the malignancy data, which consists mainly of leukemics, in more detail. There have been several reports on the elevation of urinary BAIB in leukemia and cancer. (*Fink* [1951], *Fink*, *Henderson* and *Fink* [1951], *Ishihara*, *Komori* and *Iida* [1951], *Ishihara* and *Komori* [1952], and *Gartler* and *Werthamer* [1956].) Their results have been in general agreement and we shall consider their three main aspects collectively. (1) All report a markedly increased frequency of patients with high BAIB urine concentration, the percentages ranging from about 70% in the work of *Ishihara* and his associates to approximately 25% in *Gartler*'s and *Werthamer*'s investigation of leukemics (table 5). There appears to be no relationship between differential diagnosis and the level of BAIB excretion. The only indication of any relationship between elevated BAIB urinary concentrations in the malignancies and genetically determined high excretion is in the work of *Fink*, *Henderson* and *Fink*

[1951], in which they report a high excretor in their control series who later came down with a small primary fibrosarcoma on the leg. (2) In general, the patients exhibiting elevated BAIB levels also show marked daily fluctuations in BAIB excretion. These fluctuations in some cases appear to be correlated with clinical signs or therapy; in other cases, however, there is no apparent correlation whatsoever. Finally, the third finding is that the plasma level of BAIB in these patients appears to be normal and this result seems highly significant. For if these patients were normally low excretors with a relatively high renal threshold for BAIB, then, in order for them to excrete large amounts of BAIB, their renal threshold would have to be exceeded by elevating the plasma level. Of course, it is possible in some of these cases that the disease or a particular therapy (e.g. urethane) affects the kidney directly and lowers the renal threshold. However, in a disease like leukemia, in which the rate of nucleic acid catabolism is greatly affected, it does not seem likely that such an explanation could account for all the observations.

Table 5. Urinary BAIB Concentration in Leukemics.

Age	No.	BAIB Excretion High	Low	% High Excretors	% High Excretors control group
Adults	21	4	17	20	6
Children(<15 years)	8	2	6	25	6

It should be clear from this excursion into possible relationships between BAIB excretion and various pathological conditions that causally, urinary BAIB excretion may be very complex, and that the problem of differentiating between various causes in certain instances (e.g. leukemia) is as yet unsolved.

Finally we would like to consider briefly the possible adaptive value of BAIB excretion in a much broader sense of the term adaptive, that is, with regard to its ecological significance. Although we have emphasized the fact that increased excretion of this substance occurs in certain pathological conditions, it should be pointed out that all these conditions together account for only a small percentage of the high excretors, even in white populations. Consequently we must think of β-aminoisobutyric aciduria as mainly an example of genetic polymorphism, which because of its racial and anthropoid distribution may have considerable ecological or adaptive significance. As to what the ecological significance may be, we have only speculations at this time. As an example, one might imagine that under certain nutritional conditions, say vitamin b_1 deficiency,

increased catabolism of nucleic acids may occur and under this metabolic situation, it may be advantageous for the individual to eliminate the breakdown products rapidly. This reasoning may well be premature; however, we did want to at least point out this area of the overall problem because we consider it so important and one that in many other genetic phenomena has received too little attention.

Summary

In summary we can state that in β-aminoisobutyric aciduria, we are dealing with a genetically controlled physiological variable, exhibiting marked variability in its distribution, and with some potentially important medical and ecological implications. We have attempted to discuss this phenomenon in terms of our major interest, that of the role of physiological variation in human evolution.

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SOME GENETIC IMPLICATIONS OF NILOTIC DEMOGRAPHY

By D.F. ROBERTS

In Upper Nile Province in the Southern Sudan live the peoples to be discussed, the Shilluk, the Padang Dinka (a composite name which refers to three Dinka tribes, Abialang, Ageir and Dunjol), and the Mabaan.

The wet season permanent villages of the Padang Dinka are clearly defined entities. The villages, each consisting of a cluster of huts surrounded by patches of cultivation, are separated from each other by usually a few miles of open grass and occasional scrub. The villages are spread fairly regularly over the whole tribal area; fig. 1 shows the pattern for part of the Ageir Dinka, to north and south of which respectively the pattern is continued by the Abialang and Dunjol. The village is the basic territorial and political unit: neighbouring villages are grouped into tribal segments and several such form a tribe, occupying a continuous

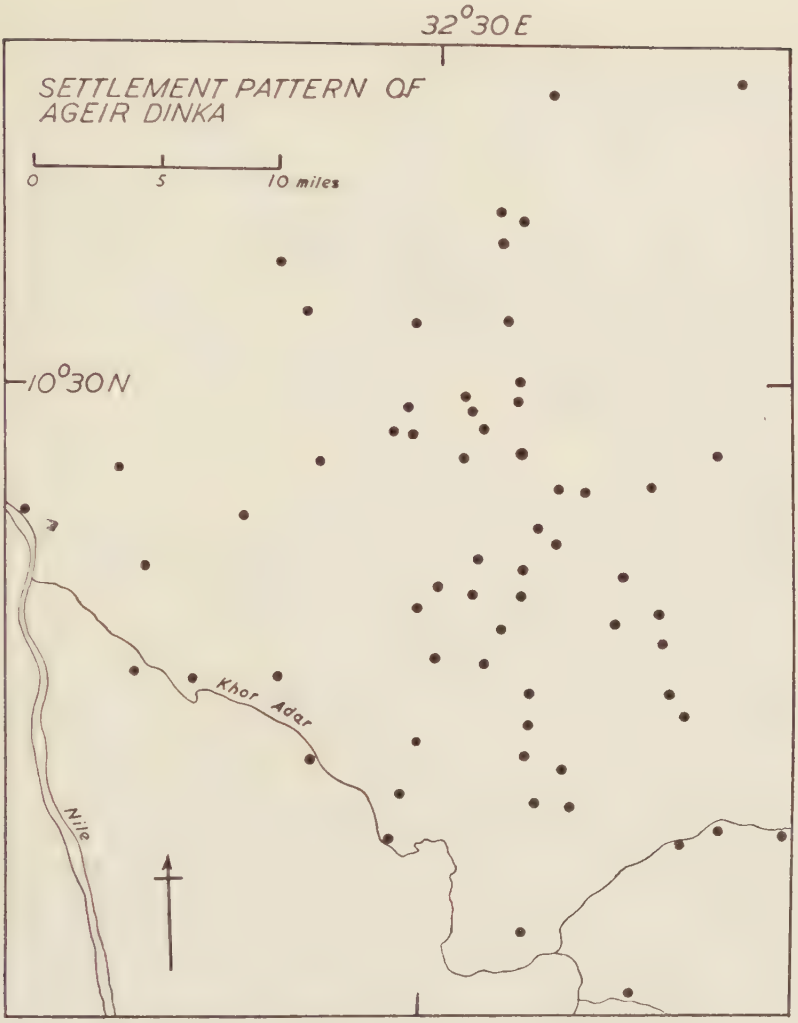

Fig. 1

territory, whose members formerly united in cases of inter-tribal disputes. Interwoven into this territorial pattern is the patrilineal clan and lineage system, which controls the mating pattern. Marriage is prohibited within the clan and its component lineages, but is allowed within more inclusive categories, provided that the participants are not closely related on the female side. Since each village is primarily the residence of members of one clan or of a lesser lineage, marriage occurs mainly between individuals of different villages.

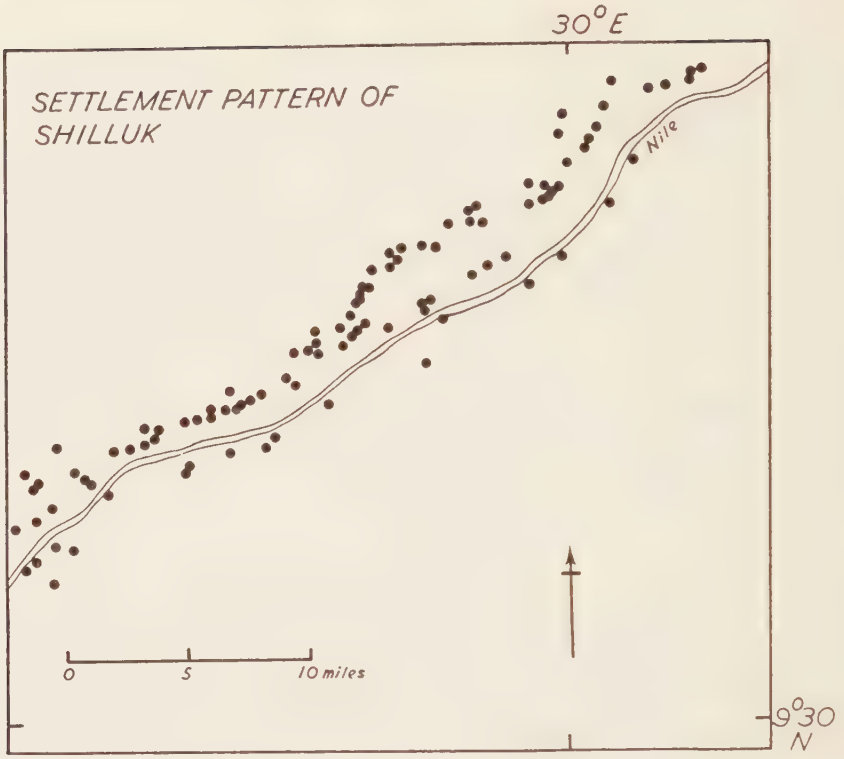

Fig. 2

Among the Shilluk marriage again is prohibited with any member of one's father's clan and between individuals closely related through the mother. The clans are however dispersed throughout Shilluk-land. Nevertheless each lineage of the clan has a definite local association. The village consists of a number of discrete hamlets, each being the residence of a small lineage. In practice, the kinship ties between neighbouring hamlets are so close that marriages within the village are not numerous. The settlement pattern (fig. 2) differs from that of the Padang, in that the villages are strung out on a ridge of firm ground that parallels the Nile and Sobat rivers, so that the Shilluk population may be regarded as existing in a number of contiguous units distributed in linear fashion.

The third population to which reference will be made is the Mabaan. Their villages lie well to the east of the territory of the Padang Dinka from whom they are separated by a belt of uninhabited country. Their villages are much smaller and much more dispersed. They apparently do not possess a lineage structure, marriage between first cousins is of frequent occurrence, and the majority of marriages occur within the village.

Little accurate demographic information exists for these peoples, the most reliable being derived from tax returns, which give an idea of the overall size of settlement units. During the course of recent investigations some more detailed information was collected concerning family size, sex, age and marital composition of the population of a village of the Abuya section of the Ageir Dinka, from which the effective population size could be calculated [1]. Also details of marriages, the geographical distances over which marriage occurs, were collected for quite a large sample covering many villages of Dinka, Shilluk and Mabaan. This information I have attempted to apply to the formulae calculated by Professor *Sewall Wright* [3, 4] relating to the genetical structure of populations, in an endeavour to see whether genetic drift is likely to occur within any of the populations.

The Island Model

The simplest model which can be set up to examine population structure has been termed the island model. A large natural population is envisaged as comprising a number of local subgroups, each breeding at random within themselves but replenished in each generation by a proportion of migrants from the total population. At first sight this model would not seem to be too diverse from the situation actually obtaining in the Dinka and Mabaan populations.

Suppose the Padang Dinka were composed of a large number of local populations each of which was of the same effective size as (a) the village investigated (109), (b) the Abuya section (380), (c) the Ageir tribe (3913). Admixture rates in the village, the section and the tribe respectively are 50%, 35% and 11%. The variance measuring differentiation due to drift of local gene frequencies in one generation in these units is respectively .0003817, .0002404 and .0001217 where the initial gene frequency is .5. The average inbreeding coefficients (F) of individuals relating to these units are respectively .001527, .0009617 and .0004866. These populations are far from approaching the level at which appreciable differentiation begins (when F increases above about .005).

The contrast from the situation seen in the Mabaan is very marked. The village taken as an example, Bontoila, was the largest of those visited, yet the effective population size is very low (21), which combined with the low migration rate gives a drift variance among villages of .007425 and an inbreeding coefficient of .02970. A small blood group sample from these Mabaan villages shows some very interesting features [2]; for instance the Lutheran positives attain a frequency of .32, the highest

value so far recorded for any population, which may well result (if selection is not operating) from the likelihood of a relatively high rate of drift.

Isolation by Distance

It may be argued that the island model in the present instance takes too little account of the movement of individuals, that the data call for analysis based on a model of continuity of individuals. The model of isolation by distance is applicable where a population occupies a territory of such an extent as to prevent panmictic mating over its whole area, so that individuals tend to marry those residing nearer to them and not those in more remote parts of the territory. The population may cover a large area (areal continuity) or may be distributed along a narrow strip (linear continuity), conditions exemplified respectively by the Padang Dinka and the Shilluk. With linear continuity the distribution of parental birthplaces relative to the birthplace of progeny is assumed to be represented by a normal probability curve, while with areal continuity the distribution is bivariate normal. Density of the populations is assumed to be uniform over the whole territory.

The properties of such populations depend on the effective population size of neighbourhoods and the system of mating. Of the four systems of mating analysed by *Sewall Wright*, three have been applied to the present data. The first relates to a monoecious population with equal dispersion from male and female parents; mating within neighbourhoods is random, except for the effect of distance. Case 2 relates to separate sexes in which reproduction is wholly by permanent pairs and the amount of dispersion of males and females is the same; this case is possibly more appropriate in the present analysis. Case 3 relates to a hermaphroditic population in which dispersion is by gametes of only one sex, included in the present analysis because of the essentially patrilocal system obtaining amongst these peoples, as the following table of the variances of parental distance in the two populations shows:—

	Father	Mother
Shilluk	28.5	463.8
Dinka	14.9	174.2

Considering first the Shilluk, in the first case of a monoecious population, assuming equal dispersion of male and female parents, with no self-fertilization, neighbourhood size is 9191 individuals, the correlation (E) between gametes of adjacent individuals is .00012565, giving for an initial gene frequency of .5 a variance due to drift among neighbourhoods

in one generation of .00003141. In the second case of permanent pairs, separate sexes, equal dispersion of male and female parents, and no brother/sister mating, the neighbourhood size remains the same, E is .00012567, and drift variance among neighbourhoods is .00003142. In the third case, assuming no dispersion of male parents, but the observed dispersion of female parents, with self-fertilization only at random, the neighbourhood size is reduced to 8740 individuals, the correlation between gametes of adjacent individuals is .00013070 and the variance .00003267.

For the Dinka, in the first case of a monoecious population, assuming equal dispersion of male and female parents, with no self-fertilization, neighbourhood size is 1409 individuals, the correlation between gametes of adjacent individuals is .0008101, giving a variance due to drift among neighbourhoods in one generation of .0002025. In the second case of permanent pairs, separate sexes, equal dispersion of male and female parents, and no brother sister mating, the neighbourhood size remains the same, E is .0008109, and drift variance among neighbourhoods is .0002027. In the third case, assuming no dispersion of male parents, but the observed dispersion of female parents, with self-fertilization only at random, the neighbourhood size is reduced to 1302 individuals, the correlation between gametes of adjacent individuals is .0009410 and the variance .0002353.

Discussion

It is quite clear that genetic drift in Dinka and Shilluk is, by reason of their marriage pattern and density of population, unlikely to be an appreciable influence of local variation of gene frequency within each population. It is only when smaller more dispersed peoples such as the Mabaan are examined that drift may be invoked as an explanation of local variations in gene frequency.

It is instructive to compare the present figures with *Sewall Wright*'s [5] diagrams of inbreeding coefficients measuring isolation by distance in populations of different sizes. For an areally distributed population such as the Dinka with a neighbourhood size of just over 1000, it is clear that even if the total population is of the order of 10 [1] drift will remain negligible. For a linearly distributed population such as the Shilluk, where the neighbourhood size is just below 10,000, differentiation of neighbourhoods only begins to become important when the total population is of the order of 10^7.

Reverting to the social structure of Shilluk and Dinka mentioned at the outset, each seems to be characterized by outbreeding, so that the

calculated figures for the inbreeding coefficients and drift variance are all to be regarded as maximal, and they may well be less. The extent to which they are exaggerated is difficult to determine, for the lineage for many is *not* a true record of paternal descent but merely a peg on which the individual hangs his activities and behaviour, so that outbreeding is perhaps less than might at first seem. Certainly for those bloodgroups where the heterozygote is phenotypically discernible there seems to be no increase of heterozygosity over that expected [2]. For the Mabaan the paucity of sociological information makes it difficult to decide the direction in which the figures err; they may well be too low.

In this work many important assumptions have been made; for instance the figures for the total population and population density are not as accurate as could have been hoped, it may not be legitimate to apply the relationship between effective and total population sizes found in one village to the tribe as a whole, the effect of Dinka seasonal migration or occasional marriage with other peoples have not been taken into account. But it seems that the errors involved are of a magnitude hardly likely to affect the general conclusions of the insignificance of drift within Dinka and Shilluk. This work however does suggest that the biological study of human populations, many of whom even today approximate the zoologists' "wild population", may be of some significance in the advance of general genetical theory. Some of the basic postulates underlying the mathematical work, for example the relationship between the variances of location points of different ancestral generations, could easily be examined. For the human group is able to provide a wealth of information not available in populations of simpler more frequently studied organisms.

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Discussion:

H. Lehmann (London): I would like to ask Dr. *Roberts* whether his calculations take into account that several marriages in his population are polygamous?

D. F. Roberts (Oxford): No. The extent of polygamy seems insufficient to affect the general conclusions, however.

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HAEMATOLOGICAL INVESTIGATIONS AND THE ORIGIN OF THE MALAGASY OF MADAGASCAR[1]

By R. SINGER and P. BRAIN

Studies of the incidence of sickling and of the blood groups in Madagascar and African populations indicate a far closer link between these populations than has previously been suggested. Although the language and culture of the Malagasy are of Malayo-Indonesian origin, genetic studies show that the African element predominates in most of the tribes.

Reference is made to the close asssociation between human migrations and the distribution of domestic animals, and knowledge of the origins of some ethnic groups may be increased by further genetic studies of this type.

[1] Full report is being published in American Journal of Physical Anthropology under title: "Physical Features, Sickling and Serology of the Malagasy of Madagascar" by *R. Singer, O. E. Budtz-Olsen, P. Brain* and *J. Saugrain.*

Sachs, L. and *M. Bat-Miriam:* Acta genet. *6*, 454, 1956/57

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FINGER PRINT PATTERNS IN JEWISH POPULATIONS IN ISRAEL

By L. SACHS and M. BAT-MIRIAM

A study has been made of the distribution of finger print patterns in Jews that have come to Israel from Bulgaria, Egypt, Germany, Iraq, Morocco, Poland, Turkey and Yemen. Five hundred males in each of these eight Jewish populations have been examined for the frequencies of whorls, loops, and arches on the ten different fingers. The analysis of this data on 40,000 fingers has shown that these Jewish populations have striking similarities in the frequencies of these genetic characters.

Discussion:

G. A. Harrison (Liverpool): Dr. *Sachs* implies that since the widely dispersed Jewish populations he has studied are more similar to each other than to surrounding populations in finger print patterns the latter are non-adaptive. Even if this particular character is non-adaptive (which I admit would be difficult to demonstrate) it is highly unlikely that its genetic basis is not maintained by selection. Polygenially determined characters as shown in the laboratory and as expected on theoretical grounds can respond very rapidly to selective forces: indeed the very fact that a character has a multifactorial basis suggests that it has been subject for a long time to varying and strong selective forces. I know only too well the dilemma of the anthropological looking for ethnic markers: if there are any neutral genes they drift, when adaptive they change with selection.

Soliman, M.A.: Acta genet. *6*, 455–462, 1956/57

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BLOOD GROUP GENE FREQUENCIES IN THE EGYPTIAN PEOPLES AND THEIR RACIAL ORIGINS

By M.A. SOLIMAN

Egypt, the gift of the Nile as Hirodotus called it, is situated in the northeastern corner of Africa. Human population is known to have been in Egypt since a time irretrievable in the history of the world. Even before the Nile itself began to hollow its channel from its origin in the southern Soudan northwards to the Mediterranean, the vast plateau which is now more or less barren, was known to be fertile and productive soil, through plentious rains which are now no longer known. On this now bare and windswept desert plateau, there once dwelt a race of men many thousands of years before the beginning of the well known ancient Egyptian civilisation around the Nile channel. This prehistoric race of men, if we can call it so, left as evidence of its existence, vast numbers of rude flint implements scattered upon the surface of the present desert exposed by the denudation.

The predynastic era also, left vast numbers of evidences of its existence particularly in Upper Egypt, where excavations were easily done in the sand of the desert.

The Delta of the Nile, however, is unfortunately so deeply overlaid with deposits of Nile mud, that the material remains of its earliest civilisation are buried forever from our reach, and it was practically impossible to find more than a small number of such evidences. Still, it is definitely known that civilisation did occur in the Nile delta before the dynastic period, and this civilisation was probably earlier and more advanced than that of the valley above. Already in the forty third century before Christ, the men of the Delta have discovered the year of 365 days, and they in-

troduced the calendar solar year, abandoning the lunar month altogether and substituting for it a conventional month of thirty days. They divided the year into twelve of these 30 day months and to complete the year to 365 days added a sacred period of 5 days at the end of the year.

The year began with a fixed date and that was the day when Sirius first appeared on the eastern horizon at sunrise as determined in the latitude of the southern Delta (Heliopolis) where these earliest astronomers lived, 4241 years B.C. It is the civilisation of the Delta therefore, which furnishes us with the earliest fixed date in the history of the world.

As regards the people who began the ancient Egyptian civilisation, much is known about their history since king Menes united the two parts of Egypt, Upper Egypt and the Delta of the Nile, and began the so called "Dynastic Time".

The geographical situation of the land of Egypt is of great importance to the study of its original races. The Nile which created the valley home of the early Egyptians rises three degrees south of the Equator, travels a long course till it flows into the Mediterranean 31 $^1_2$ degrees of north latitude. In six different places throughout its course below Khartoum, the rocks are piled in scattered and irregular masses in the stream, producing the so called "Cataracts". These rocks interfere with navigation most seriously in the region of the first, second and forth cataracts, otherwise the river is navigable almost throughout its entire course.

The Egyptian world thus was sharply defined as a deep narrow valley of unparalleled fertility, winding between lifeless deserts, furnishing a remarkable environment not to be found elsewhere in the world. The situation offered by this narrow valley was one of unusual isolation; on either side vast desert wastes, on the North the harbourless cost line of the Delta and on the south the rocky barriers of successive cataracts preventing fusion with the peoples of inner Africa.

It was chiefly at the two northern corners of the Delta that outside influences and foreign elements, which were always sifting into the Nile valley, gained access to the country.

Through the eastern corner, it was the prehistoric Semitic population of neighbouring Asia, who forced their way in across the dangerous intervening deserts. This early invasion of the Nile valley by the Semitic nomads of Asia stamped its essential character unmistakably upon the earliest strata of the Egyptian language which in structure is semitic. The semitic immigration from Asia occurred thus in an epoch far below our remotest historical horizon. The most probable route of that invasion is the isthmus of Suez along which route we may observe repeated

examples of such invasions in the historic age of Egypt. The most recent of these, was the influx from the deserts of Arabia during the Moslem invasion, about 13 hundred years ago.

Through the western corner, the Libian race of possibly European origin, found entrance to the country. Throughout the whole length of the historic age of Egypt, the Delta was open to inroads of the Libians who dwelt upon the west of it, and the constant influx of people from this source gave the western Delta a distinctly Libian character, which it preserved even up to the present time.

The products of the south also, inspite of the cataracts, filtered in ever increasing volume into the region of the lower river and the lower end of the first cataract "Asswan" became a trading post where the negro traders of the south met those of Egypt.

The natural boundaries of Egypt, however, always presented sufficiently effective barriers to would—be invaders, thus enabling the natives to assimilate the new-comers slowly, without being displaced.

The racial history of Egypt has been directly studied, first through the monuments and crafts of Ancient Egyptians and later through the anatomical study of Ancient Egyptian bodies and remains.

Before *Elliot Smith* made his most important study of the human remains excavated by the Egyptian Government in Nubia 1907–1911 no scientifically based theory was known of the racial origin of the Egyptians. A great number of contradictory hypotheses concerning this matter was prevalent; and most of the known racial groups of human beings (eg. Libyans, Negroes, Arabs, Mongols, Indians, and even red Indians and aboriginal Australians) were supposed to have come in remote times to the Nile valley and to have thus participated in the production of the worthy Ancient Egyptian.

Elliot Smith, however, armed with scientific anatomical evidence, disposed of the confusing unwarranted speculations of earlier writers and outlined the racial history of the country in a clear and simple way, which proved to be a sound basis for the study of the racial origin of Egyptians. He recognised a uniform homogeneous physical type of man which inhabited Upper Egypt and Lower Nubia in predynastic times. But he further added [1911], after the discovery of a large necropolis at Giza, which dates from the old empire, that some of the remains were distinct by having bigger and especially broader skulls, finer features and generally more robust skeletons, and to his mind these were sufficient criteria for establishing in the remains of Ancient Egyptians the reality of certain physical traits distinctly foreign to Egypt. Fortunately, *Elliot*

Smith gives, besides the anatomical description of the material, statistical constants for three characters ; and the results of statistical examination of his data, made by *Batrawi* [1940] completely vindicate his conclusion regarding the heterogeneous nature of that particular series. A comparison between the statistical constants of the two types, described by *Elliot Smith*, leaves no doubt that the two samples represented very closely related populations.

Morant [1925] studied the cranial measurements already described, and arrived at a conclusion similar to *Elliot Smith*'s but simpler and more sound. He recognised two indigeneous types of human being, the Upper and Lower Egyptians which represent the extremes of the pure native Egyptian population from early predynastic times till now. The study of the available measurements of the modern Egyptian population all over Egypt conforms closely to the Ancient predynastic Southern Egyptian type. As example of types which were entirely unaffected for several thousand years by any influences foreign to their country the Ancient Egyptians may well be unparalleled in the history of the world.

The study of the distribution of the blood group genes amongst present day populations of the whole world, has been successfully used in anthropological work. It is not my intention, in front of this distinguished audience to discuss the relative advantages of the use of blood group characters as compared with other physical characters as means of classification of mankind. But I should like to say that the study of this distribution among present day Egyptians adds an important piece of knowledge to the racial history of Egypt.

A large number of data has been published about the distribution of blood groups in different parts of Egypt. The following table shows some of these data, which fulfil *Bernstein*'s equation.

From this table it is remarkable that the gene frequencies all over Egypt and amongst holders of the two main religions, are closely similar, only few frequencies show significant differences. This can be taken safely as evidence of the homogeneity of the Egyptian population.

The Asswan sample provides the greatest frequency for "O" and the smallest for "A", the people there actually differ from most of the Egyptians, not only in blood group gene frequencies, but also in skin colour, in the shape of the hair, in the body and skull measurements as well as the language, which is also somewhat different to all the other Egyptian dialects. The high "r" value of these people is an indication of the African blend which participated in the production of our people of the south.

Sample	Observer	Number Tested	Groups				Genes		
			O	A	B	AB	p	q	r
Alexandria	Partheniades	460	30.4	48.7	14.1	6.7	0.338	0.116	0.553
Sharkia	Matta	1121	31.2	35.7	25.8	7.3	0.245	0.182	0.560
Sharkia, Arabs	Matta	86	41.9	31.4	17.4	9.3	0.229	0.143	0.646
Cairo, Moslems	Boyd	502	27.3	38.4	25.5	8.8	0.288	0.203	0.523
Cairo, Moslems	Matta	655	27.0	35.0	27.0	11.0	0.265	0.213	0.520
Cairo, Copts	Matta	418	35.5	34.3	22.0	8.2	0.242	0.165	0.596
Cairo, Copts	Moharram	1467	31.2	33.9	24.7	10.3	0.247	0.188	0.559
Cairo, Medical Students	Gohar	240	25.0	35.0	28.0	12.0	0.272	0.230	0.500
Cairo, W. R. Pts.	Gohar	300	24.0	31.0	32.0	13.0	0.252	0.258	0.490
Assiut, Moslems	Boyd	106	28.3	34.0	27.3	10.4	0.254	0.211	0.532
Assiut, Copts	Boyd	419	24.6	34.4	31.0	10.0	0.254	0.169	0.496
Asswan		500	57.5	18.5	12.9	11.1	0.161	0.128	0.755
Troups	Safty	6335	30.8	34.4	25.5	9.3	0.250	0.193	0.555
Troups, Moslems	Safty	2538	29.0	35.8	25.8	9.4	0.260	0.195	0.539
Troups, Copts	Safty	366	26.0	37.7	25.4	10.9	0.283	0.202	0.509
Various Places	Moharram	500	28.2	33.6	25.2	13.0	0.270	0.214	0.531
Various Places	Moharram	1000	31.0	32.5	24.4	12.1	0.256	0.203	0.557
Various Places	Shousha	508	27.0	32.1	24.5	16.5	0.280	0.230	0.518

It is also evident that the Alexandria sample shows a significantly high "p" value, much higher than anywhere else in Egypt. This high "p" value is also definite evidence of western admixture, Alexandria being the port of entry of any western population.

In contradistinction to the previously mentioned two ports of entry of foreign races to Egypt, the eastern port viz. Sharkia does not show any significant effect of foreign invasion on the blood group gene frequencies of its population. This fact could not be taken as evidence against the occurrence of eastern invasion to Egypt, as this invasion is well known in the history since the predynastic period till now. On the other hand, invasion of Egypt from the east is by far the most abundant in the history. At least two heavy Asiatic invasions swept into Egypt from the east, the first well known one occurred more than three thousand years ago, when the Hyksos overpowered the ancient people of Egypt and occupied the whole country for about a hundred and fifty years. Although the Hyksos invasion of Egypt is the earliest historical one known, yet the Semitic immigration from Asia occurred in an epoch that lies far below our remotest historical horizon. The second heavy influx of asiatic races to Egypt took place a little more than a thousand years ago, when the Islamic invasion entered the country. Both these invasions, together with an innumerable number of smaller and irregular filtrations of Asiatic

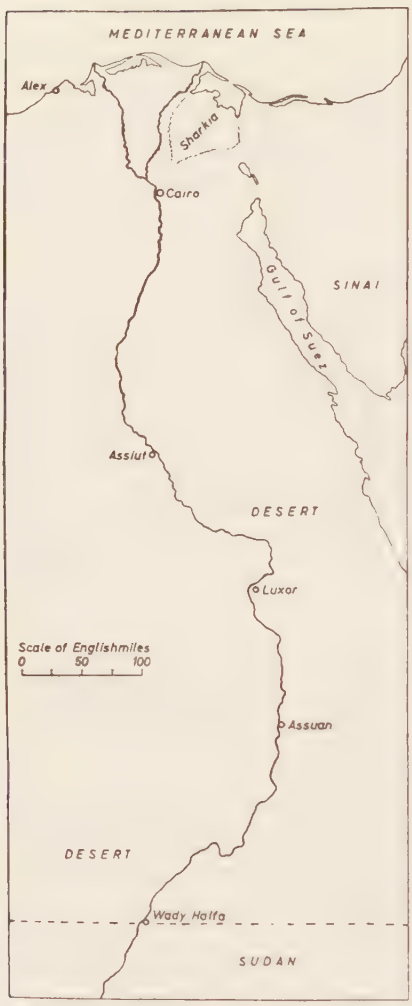

Fig. 1

people took place through the isthmus of Suez and Sharkia district, the most eastward parts of Lower Egypt. The accompanying map of Egypt shows these places.

So, although Sharkia district is the port of entry of the most abundant foreign immigration into Egypt, yet the blood group gene frequencies of the people there show a little difference from the distribution amongst other Egyptians, as seen in the following table.

That the invasion of Egypt by the Hyksos about 35 hundred years ago left no stamp of its existence on the inhabitants of the Nile Valley was once explained by the fact that the Hyksos were completely driven out of Egypt at the start of the eighteenth dynasty. This explanation is quite difficult to perceive, if one sees how difficult it is to drive a whole race completely out of a country after they have lived and mixed with its population for about two hundred years.

Even if we take this explanation as plausible for the Hyksos invasion, no such explanation can be given for the more recent influx from the deserts of Arabia in the Mohammedan invasion.

The only explanation which thus could be given for the absence of change on the population of Egyptian Sharkia is that the wandering

Sample	Number Studied	Groups				Genes		
		O	A	B	AB	p	q	r
Sharkia . .	1121	31.2	35.7	25.8	7.3	0.245	0.182	0.560
Cairo . . .	3916	29.6	35.0	25.4	10.0	0.258	0.196	0.544
All Egypt .	2425	28.4	32.7	25.4	13.5	0.267	0.218	0.533

immigrants from the east were similar to the native population of Egypt. This similarity could be clearly demonstrated by comparing the blood group gene frequencies of Egyptians with those of the eastern Arabs of Syria, which is shown in the following table.

Sample	Number Studied	Percent in Group				Genes		
		O	A	B	AB	p	q	r
All Egypt .	2425	28.4	32.7	25.4	13.5	0.267	0.218	0.533
Sharkia . .	1121	31.2	35.7	25.8	7.3	0.245	0.182	0.560
Syria (Arabs) .	1149	38.0	34.0	20.0	8.0	0.238	0.152	0.616

This table further shows the gradation between the Arab sample and the Egyptian sample with the sample of Sharkia taking an intermediate situation between both. The p and q values are highest in Egyptians and lowest in Arabs, while the reverse is true for the "r" value and the figures of the Sharkia population lie in between the two extremes.

Much has been said about racial differences between the holders of the two main religions in Egypt, Moslems and Copts. The blood group gene frequencies, however, show no significant difference between the two peoples and this is also the same with other physical anthropological measurements, which further show close similarity between the Egyptian peasant of to-day, Moslem or Copt and the predynastic Egyptian who inhabited the Nile Valley.

The following table shows the blood group gene frequencies amongst Moslems and Copts all over Egypt.

Sample	Number Studied	Percent in Group				Genes		
		O	A	B	AB	p	q	r
Moslems in Cairo . .	1911	26.9	34.3	26.6	10.2	0.269	0.218	0.519
Copts in Cairo	2005	32.2	33.8	24.2	9.8	0.249	0.188	0.567
Moslems in Assuit . .	106	28.3	34.0	27.3	10.4	0.254	0.211	0.532
Copts in Assuit. . . .	944	25.0	34.2	30.8	10.0	0.253	0.231	0.500
All Moslems	3138	27.5	35.9	26.4	9.2	0.266	0.206	0.524
All Copts	2949	29.8	33.9	26.3	9.8	0.251	0.202	0.546
All Egyptians	2425	28.4	31.7	25.4	13.5	0.267	0.218	0.533

The Cairo sample shows the highest difference and this could be easily perceived if one knows that the Cahirians are particularly liable to be more mixed with other races like Turks.

Although it is reasonable to suppose that the Moslems are more liable to be a blend of the Ancient Egyptian race and the Arab race coming with the Islamic invasion, yet the blood group gene distribution does not show any effect of admixture amongst the Moslems which is not found among the Copts. But it should be noted that the Arab invasion to Egypt although usually described as being massive, yet as already said, the invaders were rapidly assimilated by the native population without the latter being replaced or even much affected.

The distribution of the M and N, P and p, S and s, is more or less similar to most other races, thus of little value in such a study.

The Rh genes however, although of expected great value in the subject, yet the data about these genes amongst Egyptians are far from being of value in the formation of an opinion as regards the correct frequency of each gene amongst present day population.

Summary

The frequencies of the blood group genes amongst Egyptians from different districts and holding different religions are computed. Close similarity is noticed, with a significant deviation in only two districts, thus giving evidence to the homogeneity of the population. The high "p" value in Alexandria is probably due to western invasion: in the same way as African immigration in the south raised the "r" value among Nubians.

Eastern immigration, however, which is by far more abundant and frequent in the history of Egypt, shows little effect, if any on the gene frequencies. This is due to the close similarity and probably, the identical racial origin of the native Egyptians and the eastern Arab immigrants.

Among the holders of the two main religions in Egypt, Islam and Christianity, no discernible difference in the gene frequencies is found either in Cairo or in Upper Egypt. This is quite in agreement with physical anthropological measurements, which also prove that the Egyptian "Fallah" of to-day, Moslem or Copt, is very much like the predynastic peasant inhabitant of the Nile Valley.

Twiesselmann, F.: Acta genet. *6*, 463–464, 1956/57

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LES PROPORTIONS DU CORPS PENDANT LA CROISSANCE CHEZ LES MULÂTRES BELGO-CONGOLAIS

Par F. TWIESSELMANN

Les variables suivantes ont été confrontées dans leur comportement relatif pendant la croissance : la stature, la hauteur à l'épine iliaque antéro-supérieure, la longueur du bras, le diamètre bicrète et le diamètre biacromial.

La méthode de représentation des proportions corporelles des mulâtres consiste à disposer la valeur individuelle du mulâtre et d'un enfant belge témoin sur des graphiques de croissance allométrique représentatifs de la population de Léopoldville et de la population belge.

Pour aboutir à ce mode de représentation, il a donc été nécessaire d'établir d'abord les courbes de croissance allométrique pour les deux populations congolaise et belge qui servaient de base de comparaison au mulâtre et à son témoin.

Un examen comparatif de la croissance des différentes dimensions du corps par rapport à la stature a été exécuté en utilisant la formule devenue classique de croissance allométrique $\log y = \log b + \alpha \log x$. Il a été montré que :

1. la longueur du bras est, à taille égale, supérieure en moyenne chez les enfants et adolescents noirs à celle des Blancs (Belges, Américains, Italiens et Allemands) ;
2. le diamètre bicrète est, chez les Noirs, beaucoup plus petit que chez les Blancs à taille égale ;
3. la longueur des jambes, exprimée par la hauteur à l'épine iliaque antéro-supérieure, est légèrement plus élevée chez le Noir pendant toute la croissance.

Ces constatations permettent donc de penser que, les populations examinées étant de genre de vie et de milieu social différents, les diffé-

rences manifestes dans le génie de croissance des Blancs et des Noirs doivent être liées à l'hérédité.

C'est pourquoi il a paru légitime de construire des graphiques rapportant aux courbes de croissance les valeurs individuelles des mulâtres et de leurs témoins.

Le résultat essentiel qui apparaît à l'examen de ces graphiques où le diamètre bicrète sert de base de comparaison, c'est que les enfants témoins belges se groupent autour de la ligne de croissance moyenne établie pour la population générale; les mulâtres voient leurs valeurs décalées vers la courbe des Noirs, sans que leur droite de croissance moyenne coïncide avec celle des Noirs. Autant que nous le permet le petit nombre de sujets examinés jusqu'ici, on peut estimer que le graphique de croissance allométrique longueur du bras / diamètre bicrète est celui qui a le plus de pouvoir de séparation entre Métis et Européens. La croissance de la taille épine iliaque antéro-supérieure par rapport au diamètre bicrète a un pouvoir de séparation moindre, bien que les plus "Europoïdes" des mulâtres n'atteignent pas la courbe de croissance moyenne des Belges. Les relations du diamètre biacromial et du diamètre bicrète sont plus délicates à définir: on peut, en effet, penser que les relations diffèrent selon le milieu et les conditions de vie générales offertes aux groupes que l'on compare dans la même population.

En résumé, les principales dimensions squelettiques des mulâtres pendant la croissance se rapprochent davantage de celles des Noirs que de celles du progéniteur européen. La dispersion des points des valeurs individuelles des mulâtres sur les graphiques de croissance allométrique représentant la croissance des Européens et des enfants de Léopoldville montre que la courbe de croissance des mulâtres est plus proche des proportions nègres.

Discussion:

D. F. Roberts (Oxford): The difference in growth curves between European and African populations demonstrated by Professor *Twiesselmann* is in accordance with the relationships generally found between the body morphology of indigenous peoples and their climatic environments. In adults, the linear anthropometric measurements of the body are positively, and the girths and diameters negatively, correlated at highly significant levels with the mean temperatures of the habitat – correlations which have been interpreted as indicating the applicability to man of the zoological "laws" named after *Bergmann* and *Allen*.

While it is possible that these relationships are in part genetically derived, there is evidence from animal studies that they are also partly phenotypic in origin, i.e. that the body morphology depends in part on the environment in which the animal grows. Comparison of Professor *Twiesselmann*'s hybrid growth curves should therefore preferably be made with those of European and African populations *both* resident in Africa.

Wilhelm, O. und *L. Sandoval:* Acta genet. 6, 465–470, 1956/57

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BLUTGRUPPEN UND GENEALOGIE DER OSTERINSEL-BEVÖLKERUNG

Von O. WILHELM und L. SANDOVAL

In unserer Arbeit «Vorläufige Mitteilung über die Serum-Anthropologie der Osterinsel-Bevölkerung» [4] haben wir über die bis zum Jahre 1944 bereits gemachten Blutgruppenbestimmungen berichtet.

Später während unserer in den Jahren 1954 und 1956 gemachten Reisen auf die Osterinsel, war es uns möglich, diese anthropologischen Arbeiten in Verbindung mit der Genealogie der Osterinsel-Bevölkerung, die bereits 1934 begonnen war, zu ergänzen. Dank der wertvollen Mithilfe unserer Freunde *Juan Tepano*, seiner greisen Mutter *Veri Amo*, des Paters *Sebastian Englert* und *Mariana Atan*, ist es uns möglich, eine Übersicht über die Genealogie der Osterinsel-Bevölkerung bekanntzugeben und demzufolge die Resultate der bis jetzt durchgeführten 200 Blutgruppenbestimmungen zu bewerten.

Bereits im Jahre 1934 fanden wir unter den 456 Einwohnern nur 59 Personen, die ausschließlich reine Osterinsel-Abkömmlinge waren, und im Januar 1956 gehören von den 895 Einwohnern nur 128 Personen den Nachkommen der alten ursprünglichen Inselbewohner an. Die Liste dieser 128 auserwählten Personen haben wir Dr. *Emil Gjessing*, dem Arzt der von *Thor Heyerdahl* geleiteten norwegischen archäologischen Expedition, zwecks ihn interessierender anthropologischer Studien ausgehändigt.

Über die Abstammung der ersten Ureinwohner der Osterinsel bestehen bis heute nur Vermutungen; denn noch ist kein beglaubigter Beweis erbracht worden, welches die ersten Bewohner dieser Insel waren, noch woher sie kamen. Die zahlreich ausgeführten Arbeiten und die augenblicklich gemachten interessanten Nachforschungen sind es gerade, die dazu bestimmt sind, dieses Rätsel zu lösen.

Die Ankunft des Königs Hotu Matu'a, welcher von Hiva (einem Kontinent) auf die Insel kam, muß zu den feststehenden Tatsachen gerechnet werden. Taene Arai, der Vater Hotu Matu'as, war ebenfalls König eines auf kulturell hohem Niveau stehenden Volkes, wie es seine Gebräuche, seine Priester, seine Schrifttafeln (mit Bustrofedon-Schrift), Samen, Knollen, Geflügel, Werkzeuge und die mustergültige Besiedlung der Insel bezeugen. Hotu Matu'a kam mit einigen Hundert Untertanen auf zwei großen Schiffen an.

Die Zeit der Ankunft Hotu Matu'as und die Kolonisierung der Insel durch diesen König wird in Verbindung mit den genealogischen Aufzeichnungen der Ariki errechnet; es hat aber keinen Zweck, über die von den verschiedenen Autoren angegebenen Zeitabschnitte zu diskutieren, solange die Resultate der mit der C_{14} Methode bewerkstelligten Nachforschungen, welche über das genaue Alter des organisch archäologischen Materials Aufschluß geben, nicht bekannt sind.

Aus der Nachkommenschaft des Königs Hotu Matu'a und seiner Angehörigen (Söhne und Enkel) sind die acht wesentlichsten Volksstämme hervorgegangen: Miru; Haumoana; Ngatimo: Marama; Ngaure; Ure o Hei; Tupahotu; Koro Orongo und vier kleinere Stämme, von denen drei dem Stamm Miru angehören: die Raa, Mamae und Hitihuira, und einer dem Stamme Tupahotu: die Mokomae. Insgesamt 12 Stämme, von welchem der Miru der älteste und mächtigste war.

Die Familien, welche einen Stamm bildeten, besaßen keine eigenen Familiennamen, sondern dem Namen des Sohnes wurde der Name des Vaters angehängt und diesem wiederum der Name des Großvaters und sogar der des Urgroßvaters. Diese eigentümliche Namens- und Familiennamensgebung erleichterte es, die väterliche Genealogie während drei bis vier Generationen zu kontrollieren. Bezüglich der Zusammenstellung der Stammbäume wurde manchmal auch noch eine besonders bedeutsame Begebenheit hinzugefügt, so z.B. eine Heldentat oder ein besonderes Gewerbe, oft auch nur der Ort des Wohnsitzes.

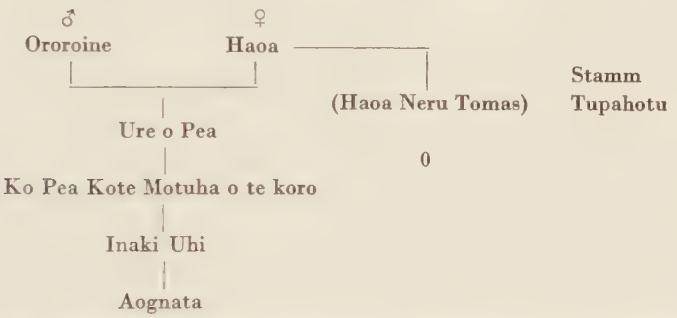
Ankunft der Hanau Eepe

Während der Regierungszeit des Ariki Tu'u Ko Iho wird eine neue historische Begebenheit von allergrößter Bedeutung vermerkt: die Ankunft der Hanau Eepe, die ohne ihre Frauen kamen. Laut Berechnungen des Paters Sebastian Englert in bezug auf die Genealogie der Arikis würde die Zeit ihrer Ankunft in den Beginn des 17. Jahrhunderts fallen. Es handelt sich um die Einwanderung eines weiteren tapferen Stammes, welchem die megalithische Baukunst der Mohais beigemessen wird. Es

war ein Stamm breitschultriger Männer (hanau = Stamm; eepe = breit, kräftig, groß) im Gegensatz zu den Hanau Momoko (Männer einer schlanken Rasse), die mit Hotu Matu'a auf die Insel kamen.

Der Stamm Hanau Eepe ehelichte Frauen des Stammes Momoko; jedoch die Feindschaft unter diesen Stämmen, durch die verschiedenartigen somatischen und psychischen Charaktereigenschaften verursacht, zeugte so tiefen Haß und Gegnerschaft, daß ein furchtbarer Rassenkampf heraufbeschworen wurde, der mit der Vernichtung des Stammes Hanau Eepe im Graben von Kote Uma Ote Hanau Eepe endete. Vom Stamm Hanau Eepe rettete sich ein einziger: Ororoine, der sich mit einer Frau der Familie Haoa aus dem Stamm Hanau Momoko verheiratete, aus deren

Genealogie der Nachkommen Ororoines.



Atamu Hare Kai Hiva	Manu Iri	Mata'u	Mata Kauva'e	Puna Hae Aro Moai	Aro Purunga
c.c. Regna Varu	c.c. Tetono		c.c. Te Oho aneru viuda de Te Pihi		
		Regna roaroa			Arakilio pua Arahoa
Atamu Tuputahi c.c. Regna Maruaki	Regna hopuhopu		Arone Rapu		
Jose Abraham Atan c.c. Hil Pakomio	Hipolito Ika y sus hermanas	Urbano Rapu	Urbano Rapu		Juan Araki
	(Ika Tuki 0) (Papiano 0)				

Mariana	Pedro	Juan	Margarita		Rapu Pua Aresenio	Araki Narez: Juan Jose	Araki Narez: Enrique
Blutgruppe 0		0	0	0	0	0	0

Monat und Jahr	Autor	Gesamtzahl Osterinselbevölkerung	Zahl der untersuchten Individuen	O		A		A_1		B		AB			
				No.	%	No.	%	No.	%	No.	%	No.	%	MN	Rh
12. 1932	*Rahm*	320	63	16	25.35	44	69.80	–	–	2	3.10	1	1.55	–	
9. 1934	*Wilhelm*	442	96	43	44.7	52	54.1			1	0.10	–	–	–	
12. 1934	*Drapkins*	456	158	59	37.34	90	56.96			5	3.16	4	2.53	–	
3. 1944	*Sandoval* *Wilhelm*		22	13	59			9	40.9	–	–	–	–	8 MN 3 N 1 M	Rh Rh
1.u.2. 1954	*Wilhelm*														Rh
1956	*Sandoval*	895	82	23	28.04	38	46.3	20	24.3			–	–		Rh
Prozentsatz der Auslese					30.7 %				69.3 %						

Verbindung viele Kinder und Enkel hervorgingen; unter letzteren figuriert Ure 0 Pea, der Urgroßvater von Atamu Hare Kai Hiva. Unter den Nachkommen Ororoines, beziehungsweise von Ure o Pea, figurieren José Abraham Atan, der sich mit Hil Pakomio verheiratete. Aus dieser Ehe stammen Pedro Atan, gegenwärtiger Bürgermeister der Osterinsel, sowie seine Brüder; Hipólito Ika und seine Brüder; Urbano Rapu und Juan Araki (siehe genealogische Tabelle).

Bei allen Nachkommen dieser Genealogie haben wir ausschließlich die Blutgruppe 0 angetroffen. Andrerseits wurde unsere Aufmerksamkeit darauf gelenkt, daß bei den Abkömmlingen der Stämme Miru, Topahotu, Marama und Raa auch eine relative Häufigkeit der Blutgruppe 0 angetroffen wird und unter der betreffenden Blutgruppe A die Heterozygoten häufig sind, besonders in den Familien Veri Veri, Teao, Araki, Narez, Fati und Pakomio.

Notwendig ist eine Revision mit der C_{14}-Methode des alten anthropologischen Materials dieser Rassen und Stämme, insbesondere der studierten und bekannten Schädel, die aus bekannten Ahus stammen.

Unsere sero-anthropologischen Studien, die mit den bis jetzt bekannten Arbeiten auf der beigefügten Tabelle eingetragen sind, beweisen, daß nach unserer genealogischen Kontrolle nur 0 und A_1 unter der reinen Osterinsel-Bevölkerung vorkommen.

Zusammenfassung

1. Die genealogische Kontrolle der augenblicklichen 895 Bewohner der Osterinsel (Februar 1956) laut Forschungen nach *Wilhelm* ab 1934, 1944 und 1954, assistiert durch *Juan Tepano* und dessen Mutter, dem Pater *Sebastian Englert* und *Mariana Atan*, zeigt, daß unter den zur Zeit lebenden Nachkommen allein 128 reine Osterinsel-Abkömmlinge sind und daraufhin das anthropologische Material zum Blutgruppenstudium geeignet ist.

2. Die von uns durchgeführten sero-anthropologischen Forschungen (96 im Jahre 1934, 22 im Jahre 1944 und 82 im Jahre 1956 = insgesamt 200 Untersuchungen), in Verbindung mit der genealogischen Kontrolle, beweisen das Vorkommen der Gruppen 0 (30,7%) und A (69,3%). Alle A gehören zu A sub 1 (A_1). Im System M.N. existiert in prädominanter Form N., wie ja bereits in der 1945 veröffentlichten Abhandlung bemerkt wurde. Von den 12 Rh-Untersuchungen aus dem Jahre 1934 und den 34 aus dem Jahre 1956, also 46, ergaben 42 Rh-positiv und 4 Rh-negativ. Die Rh sub 1 prädominieren über Rh sub 2. (In den 18 Kontrollmustern, von *Thor Heyerdahl* eingesandt an Dr. *R. T. Simmons*, Commonwealth Serum Laboratories in Melbourne-Australien, wurde KELL nicht festgestellt.)

3. Unter den Nachkommen der Hanau Eepe nach der Genealogie der Ororoine mit Haoa und Ure o Pea, innerhalb welcher die Familien von José Abraham Atan, Hipólito Ika, Urbano Rapu und Juan Araki figurieren, haben wir bis jetzt ausschließlich die Gruppe 0 angetroffen.

4. Jedoch unter den reinen Abkömmlingen der Stämme Miru, Tupahotu, Marama und Raa ruft das relativ häufige Vorkommen von 0 die Aufmerksamkeit wach und, innerhalb seiner betreffenden A, verschiedene Heterozygoten, wie wir bei den Familien Veriveri, Teao, Araki, Narez, Fati und Pakomio feststellen konnten.

Summary

1. The genealogical control of the 895 inhabitants of Easter Island (in February 1956) are studied by *Wilhelm* since 1934, 1944 and 1954 with Juan Tepanos help and his mother, of father Sebastian Englert and Mariana Atan, shows that there exist among the actual descendants only 128 which are exclusively of primitive origin, and for this reason the adequate anthropological material for the study of the blood types.

2. Of the anthropological works done by us (96 in 1934; 22 in 1944 and 82 in 1956 = 200 exams in all) related with the genealogical control,

we realize that the only groups existing O (30.7%) and A (69.3%). All the A belong to A sub 1 (A_1). In the M.N. system there is a predominance of N., as we had seen in our first publication (1945). As regards the Rh. of 12 exams done in 1934, and 34 in 1956 (46 in all), 42 were positives, and 4 Rh. were negatives. The Rh. sub 1 predominates over Rh. sub 2. In the 18 control samples sent by Thor Heyerdahl to Dr. *R. T. Simmons* of the Commonwealth Serum Laboratories in Melbourne Australia, it was demonstrated that there was no Kell.

3. Among the descendants of Hanau Eepe through the genealogy of Ororoine with Haoa and Ure o Pea in which José Abraham Atan: Hipolito Ika; Urbano Rapu and Juan Arakis families are mentioned we have found till now exclusively the group O.

4. Among the pure descendants of the following tribes: Miru, Tupahotu, Marama and Raa, our attention is drawn to the fact that there is also a relative frequency of O. and among its respective A. different heterozygotes as we have been able to establish in the Veriveri, Teao, Araki, Narez, Fati and Pakomio families.

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Aubenque, M. J.: Acta genet. *6*, 471–472, 1956/57

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A PROPOS DES STATISTIQUES GÉNÉRALES DE POPULATION

Par M. J. AUBENQUE

1. Les études de génétique humaine, et notamment de génétique de population, doivent reposer sur des données démographiques suffisamment nombreuses et précises:

a) Références *quantitatives*, démographiques proprement dites, fournissant des caractéristiques statiques de la population (nombres, structure par sexe, âge...) telles qu'elles résultent des recensements ainsi que des caractéristiques dynamiques (natalité, fécondité, mortalité, migration...) qui sont déduites des statistiques du mouvement de la population (vital statistics)[1].

b) Références *qualitatives* générales fournies par les statistiques sanitaires et médicales étendues (causes de décès, de morbidité, médico-hospitalières, médico-scolaires, de sécurité sociale etc.), par des statistiques anthropologiques, biométriques portant sur des ensembles.

2. Réciproquement la génétique, par les informations qu'elle apporte, par les modèles qu'elle propose, peut contribuer largement à l'interprétation des faits démographiques, sanitaires et anthropologiques d'ensemble (natalité, fécondité, mortalité différentielles, évolution de la fréquence des maladies, des infirmités, des causes de mort, modifications progressives des comportements biométriques, etc.)[2].

3. Le rapprochement entre les activités de statistique générale de population et les activités de génétique ne peut donc être que fructueux. Il convient d'établir des liens plus étroits entre ces disciplines.

[1] Sur les services que peuvent rendre à la génétique les concepts et les données de la démographie, on lira utilement la note de *Léon Tabah* «Génétique et démographie» (Revue «Population», 1949, 1, p. 149).

[2] Pour ce qui concerne spécialement les relations entre génétique et démographie on prendra utilement connaissance des nombreuses communications qui ont été présentées au Congrés Mondial de la Population (Rome 1954, Séance n° 23) sur les «Rapports entre l'évolution démographique et les facteurs génétiques».

4. Les études génétiques et les statistiques générales de population ont des origines historiques différentes, elles répondent à des préoccupations distinctes et même à des conceptions qui ne sont pas nécessairement concordantes. Alors que la recherche génétique répond à des préoccupations strictement scientifiques, les statistiques générales officielles sont nécessairement empreintes d'un caractère administratif comptable, d'une certaine rigidité inhérente à leur nature et nécessaire pour assurer la continuité des séries.

5. Dans le cadre de leur relative rigidité les statistiques générales doivent cependant pouvoir répondre, dans une mesure suffisante, aux besoins de l'information scientifique. Cette adéquation suppose:

a) *Une cohérence des concepts et des définitions avec les phénomènes bio-démographiques sous-jacents.* Une évolution dans ce sens est largement commencée (exemples: définition rationnelle du mort-né, normalisation des statistiques des causes de décès)[1].

b) Un *élargissement et un assouplissement des cadres qui définissent les limites de l'information apportée par les statistiques démographiques et sanitaires.* Cette extension est notamment souhaitable pour les statistiques sanitaires d'ensemble qui peuvent apporter une information étendue et systématique (sur les maladies, les infirmités...)[2]. Ces extensions peuvent être variables suivant les besoins de la recherche (insertion de questions «volantes» dans les questionnaires habituels, sondages...).

6. La cohérence conceptuelle et méthodologique doit être doublée *d'une liaison effective dans les travaux entre généticiens et statisticiens démographes et sanitaires*[3], non seulement pour assurer l'échange d'informations nécessaires mais aussi pour provoquer des progrès réciproques. Le scientifique ignore trop souvent les informations que peuvent lui apporter les statistiques officielles et réciproquement le responsable de la statistique peut ne pas connaître les besoins scientifiques auxquels ses statistiques ont éventuellement à répondre.

7. Cette collaboration suppose des *formations techniques pourvues d'ouvertures suffisamment larges sur des domaines connexes.*[4]

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[1] Voir «Hand book of vital statistics methods» des Nations Unies (Studies in methods, Series F, n° 7, 1955) et le «Règlement n° 1 de l'Organisation Mondiale de la Santé relatif à l'établissement et à la publication des statistiques de maladies et de causes de décès» (1950).

[2] Voir *J. Sutter* «Le facteur qualité en démographie» (Revue «Population», 1946, 2).

[3] En France l'Institut National d'Etudes Démographiques accorde une large place à cette collaboration (voir la publication de ses travaux de démographie génétique dans la revue «Population», Paris).

[4] Depuis l'année 1949 un cours à option de génétique mathématique a été introduit dans le programme d'enseignement de l'Institut de Statistique de l'Université de Paris.

Holt, Sarah: Acta genet. *6*, 473–476, 1956/57

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QUANTITATIVE GENETICS OF DERMAL RIDGE-PATTERNS ON FINGERS

By SARAH B. HOLT

During the past ten years the method of ridge-counting has been used to provide a quantitative approach to the study of dermal ridge-patterns on fingers. It has the advantage of overcoming classification difficulties encountered in qualitative analyses of pattern-types. The ridge-count, obtained from a finger print, gives an estimate of the size of a pattern and consists of the number of ridges which cut or touch a straight line running from the triradius to the core or centre. In a simple arch, where there is no triradius, there is no ridge-count. In a loop with one triradius, there is one count, while in a whorl there are two triradii and hence two counts, one from each triradius to the centre or centres of the pattern. In the latter case the higher count only has been used. By adding the ridge-counts for the ten fingers of an individual a single score is obtained, the *total rigde-count.*

Total ridge-count data have now been obtained from the finger-prints of a considerable series of unrelated individuals and family groups. The results of genetical analyses of these data are summarised here. They include recent, unpublished results obtained from combining new data from a large sample of sibs and from smaller samples of monozygotic and dizygotic twins with similar groups of previous data.

Before entering on genetical studies it was necessary to know something about the range and distribution of the total ridge-count in the general population. The range is from 0 to 285. Frequency distributions for a population sample of 825 males and 825 females are non-*Gaussian*. In each sex the distribution is negatively skew and slightly flattened. The mean total ridge-count is 144.98 (σ – 51.08) for males and 127.23 ($\sigma = 52.51$) for females. These means are significantly different.

There is a marked tendency for the right hand to have a higher ridge-count than the left. In a sample of 254 males and 240 females two-thirds of the individuals had a higher count on the right hand. However, the correlation between right and left hands is very high (0.94 ± 0.01 for males and 0.93 ± 0.01 for females).

For determining methods of inheritance in man data from parents and children, sibs and twins are necessary. For consideration of parent-child relationships ridge-count data were available for 149 families (consisting of both parents and at least one child) with 156 sons and 145 daughters. Total ridge-counts of 718 sibs (359 brothers and 359 sisters) falling into 290 sibships were used for sib-sib analyses. Data from the finger-prints of 172 twin pairs, 80 monozygotic and 92 dizygotic were also used.

In order to allow for the difference between means in males and females a simple sex correction based on this difference has been used.

To estimate the correlation, r, for total ridge-count between parents and children each child was entered twice in a correlation table, i. e. once with each parent. The value of the parent-child correlation obtained is 0.50. Using this method of entry there is no means of estimating the standard error accurately. The value of the interparental correlation, which is not significant, is 0.05 ± 0.08.

Correlations between mothers and children and between fathers and children are similar : r 0.49 ± 0.04 for the former, and r 0.50 ± 0.04 for the latter.

Neither mother-son, mother-daughter, father-son nor father-daughter correlations are significantly different from 0.5, though the difference in the case of the mother-daughter correlation (0.60 ± 0.05) is approaching the 5 % level.

The value of the midparent-child correlation is 0.69 ± 0.03.

The intra-class correlation for sibs was estimated in two ways. The first method, using an ordinary analysis of variance, gave a correlation of 0.50 ± 0.04. In the second method the correlation was estimated by a semi-weighted analysis of variance, the value obtained being 0.49 ± 0.04.

The intra-class correlation for monozygotic twins is very high, 0.95 ± 0.01, while for dizygotic twins the correlation is similar to that between sibs, viz. 0.49 ± 0.08.

From the results there is no doubt that pattern-size as measured by total ridge-count is inherited. This is shown by the highly significant parent-child and sib-sib correlations, taken in conjunction with the facts

that monozygotic twins are far more highly correlated than dizygotic and that the correlation coefficient for dizygotic twins is similar to that for sibs.

It may also be concluded that dominance is absent. Although total ridge-count is a discontinuous character, it behaves very like a continuously varying one. The correlations between parents and children and between sibs are near 0.5, the theoretical value for each when additive genes with independent effect, but without dominance, are present. Moreover, the estimated midparent-child correlation (0.69 ± 0.05) agrees well with the theoretical value of $1/2$ or 0.71, under these conditions. A further test for detecting recessivity also gives compatible results. With suitable data linear regression of offspring on the average value for the parents suggests lack of dominance, deviations from linearity being associated with dominance or recessivity, according to the direction of the divergence. The regression for total ridge-count of offspring on midparent value is linear, the value of the regression coefficient being 0.92, a good approximation to the theoretical value of 1.0 for a gene effect without dominance.

As mother-child and father-child correlations are essentially the same, there is no evidence of a maternal (environmental) effect. The very high monozygotic twin-twin correlation also points to the effect of environmental factors being small – about 5 %. Such an effect would of necessity be maternal, for only conditions *in utero* can affect the formation and alinement of dermal ridges. Presumably, the environment has effect over a short period only, as the ridges are completely formed by the end of the fourth foetal month. With the time factor-limited in this way, it is hardly surprising that the environmental effect is apparently small.

The non-normality of the frequency distributions for total ridge-count suggests that a comparatively small number of genes having appreciable effect is involved. A large number of additive genes would give a nearly normal distribution (e. g. stature). Attempts to analyse the rather complicated shapes of the distributions for males and females into 3 components, corresponding with the 3 phenotypes produced by one pair of alleles, have so fare been unsuccessful. It would seem, therefore, that at least 3 alleles, at either one locus or more than one, are involved, and probably more.

Discussion

M. Weninger (Wien): Aus den sehr exakt durchgeführten Untersuchungen von Mrs. *Holt* geht zweifellos hervor, daß zwischen den quantitativen Werten von Eltern und Kindern starke Beziehungen erblicher Natur bestehen. Ob aber die Zahlenwerte für die Korrelatio-

nen und Regression genügen, um einen bestimmten Vererbungs*modus* anzunehmen, möchte ich bezweifeln. Zunächst müssen wir uns fragen, ob die zu Grunde gelegten Merkmale einer biologischen Realität entsprechen. Schon die Gleichsetzung des quantitativen Wertes eines wirbelartigen und eines schleifenartigen Musters bedeutet eine ziemlich willkürliche Voraussetzung, über die wir freilich nicht umhin können. Die charakteristische Verteilung der quantitativen Werte auf die 10 Finger des Individuums findet durch die Annahme von additiven Allelen überhaupt keine Erklärung.

Statistische Gesetzmäßigkeiten, die sich aus der Behandlung von Gruppen ergeben, befähigen uns leider nicht, mit Sicherheit auf einen bestimmten Vererbungsmodus zu schließen, obwohl sie natürlich damit zusammenhängen.

F. Keiter (Hamburg): Some years ago I have made the same investigations in Germany. I got a better normal distribution but lower correlation coefficients.

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GENETICAL INTERCORRELATIONS BETWEEN SEVERAL DERMATOGLYPHICAL TRAITS

By J. PONS

Systematic analysis of dermatoglyphics in different human groups permits the selection of several traits useful for classification of populations. The importance of dermatoglyphics in this relation is sufficiently known. But in human genetic investigations its use is more reduced. The purpose of the present communication is the analysis of some aspects of dermatoglyphics regarding its use in human genetics, pointing out, firstly, the most striking advantages and disadvantages presented when employed for this object.

Dermatoglyphics, the differentiation of which occurs during the first months of the intrauterine life, remain constant after birth, and therefore (except in size), they do not vary with age, a factor which is considered a great advantage, in opposition to many other human traits, variations of which due to age, nutrition, the climate and other postbirth factors constitute a difficulty in the appreciation of the genetic mechanism.

Table 1. Correlation Coefficients between Palmar Areas. Pattern vestiges of the five palmar areas are included with the whole of true patterns.(——— = probability lower than 5 %; (=== = probability lower than 1 %).

	IV	III	II	Thenar + I
Spaniards of NE. (n = 347):				
Hypothenar	—0,030±0,039	+0,062±0,039	—0,084±0,037	—0,076±0,037
Thenar + I	—0,051±0,040	+0,051±0,040	+0,065±0,056	
Second area	—0,024±0,038	+0,140±0,032		
Third area	—0,682±0,030	=======		
Negroes of the Spanish Guinea (n = 1015):				
Hypothenar	—0,024±0,025	+0,018±0,025	—0,015±0,023	—0,052±0,022
Thenar + I	+0,010±0,024	+0,032±0,024	+0,071±0,027	
Second area	—0,006±0,024	+0,201±0,026	======	
Third area	—0,372±0,031	=======		

Dermatoglyphics have a genetical basis, as can easily be deduced from the analysis of families and twins, and their variations are comparatively common in the majority of populations. The number of genes involved and their interactions is, however, unknown, and the expression may be modified during the intrauterine life, up to a certain limit, as it is proved, when differences are observed between monovular twins as it happens sometimes.

A striking advantage is that there is no assortative mating, c. f. skeletal dimensions and pigmentation. Its undoubtedly multifactorial hereditary mechanism, is certainly a disadvantage if we compare it with traits of monomerical inheritance, but on the other hand, it offers great possibilities in certain studies of population genetics, for dermatoglyphics are less liable to variations of genetic drift.

It is true that the correct interpretation of their variations demands a more laborious technique than the other human traits and that the classifications of types of patterns are sometimes arbitrary up to a certain point, perhaps this will partially explain why it is less used in human genetics. If, however, we review the above considerations, it will be logical to admit that, even without attributing them superiority over traits classically used, dermatoglyphics may be useful in many problems of human genetics.

Having pointed out these particularities of dermatoglyphics it is

Table 2. Correlation Coefficients between Palmar Areas. Pattern vestiges and true patterns are merged. For the second, third and fourth interdigital areas, we only consider as "presence" of pattern the areas having vestiges and patterns with accessory triradius (——— = probability lower than 5 %; ==== = probability lower than 1 %).

	IV	III	II	Thenar + I
Spaniards of NE. (n = 347):				
Hypothenar	+0,041±0,039	—0,043±0,040	—0,084±0,037	—0,076±0,037
Thenar + 1	+0,032±0,043	—0,019±0,016	+0,065±0,056	
Second area	+0,057±0,048	+0,119±0,138		
Third area	+0,036±0,053			
Negroes of the Spanish Guinea (n = 1015):				
Hypothenar	—0,011±0,024	+0,021±0,026	—0,015±0,023	—0,052±0,022
Thenar + I	+0,024±0,024	+0,025±0,028	+0,071±0,027	
Second area	+0,163±0,026	+0,106±0,051	=======	
Third area	—0,021±0,022			

interesting to find out, and this is the principal motive of my paper, the grade of interdependence of several dermatoglyphical traits. It is well known that in studies of linkage, in disputed parentage, in racial comparisons etc., many authors consider independently the results obtained in each of the dermatoglyphical traits, and when considering the morphological and phenogenetical characteristics common to them, we can expect association between some of them. The association between traits may be determined by assortative mating, pleiotropy, linkage etc. The first can be discarded for dermatoglyphics, and, as regards the other two, it is well known that pleiotropy determines correlation in a homogeneous general population between the traits considered and the linkage results in the correlation within sibships.

In the present work, we analyze the magnitude of the possible pleiotropic relations that may exist between different dermatoglyphical traits. It is obvious the smaller these relations are, that is, the greater the independence between the different traits, the wider will be the information obtained on the whole of dermatoglyphics and therefore its importance for genetical studies is higher.

Material and Technique

We have used two series (347 Spaniards and 1015 Spanish Guinea Negroes), both including unrelated persons. The traits used are : Pattern

frequencies in the five palm aeras, i. e., hypothenar, thenar and second, third and fourth interdigital areas, as well as, the obliqueness of the palmar lines expressed by the Cummins' "main-line index" and the individual quantitative value of finger prints.

To give an idea of the magnitude of the possible pleiotropic relations we can use the correlation coefficient : for quantitative traits by calculation of the ordinary product-moment and for qualitative ones, the variability of which consists in the presence or absence of pattern (tables 2×2), we employ the coefficient V (*Kendall* [1948]). The standard error of V is obtained from the formula of variance of V due to *Yule* [1912]).

This work is a preliminary communication of a more extensive publication which will shortly appear in "Genética Iberica" of the Spanish Council of Scientific Research. In this paper we justify the use of V coefficient instead of the tetrachoric correlation and we also consider the difficulty of analysing certain aspects of those qualitative traits, the genetical basis of which is multifactorial. The difficulty is reduced when we deal with quantitative traits. For this reason we also employ the suggestion given by *Penrose* [1954] of introducing when possible, the use of quantitative measurements instead of limiting ourselves to the employment of a simple qualitative evaluation.

Results

Here we shall not consider the detailed analysis of correlations between the different areas of each region in particular, we shall only refer, in general form, to the magnitude with which the several dermatoglyphical traits are correlated.

As regards the five palm areas, we were able to verify that in both, Spaniards and Negroes, only four of the ten possible correlations are significant and generally minute. On account of technical reasons, not worth describing here, it was convenient to relate again the five palm areas inter se, and the three interdigital areas II, III and IV are now considered with "presence" of pattern only if they are provided with pattern with accessory triradius. The correlation coefficients are now smaller and significant in minor number.

As regards the fingers, the correlation between the quantitative values of the different fingers have not yet been established in our samples, but we have at our disposal the results obtained by *S. Holt* [1951] which give an idea of the magnitude of correlations in a series of 200 Britishers. The correlation coefficients are high and vary from 0,32 to

0,87. The greatest correlations are given in homologous fingers, and the adjacent fingers are more correlated than those more distant.

To conclude our present work, we have calculated the grade of interdependence existing between a dactylic trait and a palmar one, using two quantitative expressions, the individual quantitative values for the fingers (average of ten fingers) and for the palm we use the grade of obliquity of the palmar lines expressed by the Cummins' "main-line index" (*Cummins* and *Midlo* [1943]). The corresponding correlation coefficients calculated: (Spaniards, $r = -0{,}03 \pm 0{,}05$; Negroes, $r = -0{,}01 \pm 0{,}04$) indicate a complete independence between both traits.

Considering the above, we must mention, ignoring small variations of detail, that the possible pleiotropical relations between several dermatoglyphical traits of Spaniards and Negroes are similar. Nevertheless, it is convenient to complete a larger number of comparisons, not only considering the different qualitative characteristics of dermatoglyphics, but especially seeking for quantitative expressions in accordance with the criterion previously pointed out.

Summary

The dermatoglyphical configurations are not completely independent, but, between some areas there are clear relations. But ignoring the high correlation which exists between different fingers and between some adjacent palmar areas, the importance of which will be analysed in a separate publication, there is no doubt that the majority of dermatoglyphical traits behave amongst themselves with striking independence, which is far from being an inconvenience, for, the greater is the independence between the different dermatoglyphical traits, the greater will be the genetic information given by each pair of individual hand prints. This, together with the ease of obtainment and conservation, increases the interest of employment in human genetics.

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Discussion:

M. Weninger (Wien): Positive Korrelationen verschiedener Merkmale von Einzelindividuen sind weder für Pleiotropie noch für Koppelung beweisend. Gewiß wird Pleiotropie zu besonders hohen Korrelationskoeffizienten zwischen Merkmalen führen. Und ähnlich werden sich in nicht-panmiktischen Populationen bei Koppelung positive Korrelationen zeigen. Doch ist der unbedingte Rückschluß nicht möglich. Denn Korrelationen von Merkmalen können durch verschiedenerlei Ursachen bedingt sein.

Ob Merkmalsbeziehungen, die wir durch Korrelationskoeffizienten aufzeigen, wirklich genetischer Natur sind, kann nur aus Familienuntersuchungen erschlossen werden.

Harrison, G. A. and *J. J. T. Owen:* Acta genet. *6*, 481–484, 1956/57

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THE APPLICATION OF SPECTROPHOTOMETRY TO THE STUDY OF SKIN COLOUR INHERITANCE

G. AINSWORTH HARRISON and J. J. T. OWEN

Until the suitability of the reflectance spectrophotometer was recognized (*Weiner* [1952]) the only methods available for measuring human skin colour involved a visual matching with colour standards. The most widely used were *R. R. Gates*' tinted papers and the blends produced by spinning together varying amounts of differently pigmented discs (the colour top). The former suffers from the severe disadvantage that it pre-arranges the existence of distinct classes of skin colour; the latter, that it is difficult to summate the different ingredients of the blend in a meaningful measure of colour (the percentage of black was usually used). Both suffer from the disadvantage that they depend upon the visual judgement of the observer and have poor repeatabilities. The reflectance spectrophotometer on the other hand has none of these disadvantages for it gives an accurate and objective measure of skin colour on a continuous scale which can meaningfully be reduced to a single value.

Briefly reflectance spectrophotometry consists of illuminating a surface with light at different wave-lengths and measuring the amount of light reflected at each of these wave-lengths.

In the present investigation an Evans Electro Selenium Ltd. Reflectance Spectrophotometer has been used. It is designed in the form of two main units, namely a galvanometer unit and an applicator head. The applicator head is freely movable and can be applied to the skin surface in most regions. It houses a 6 volt lamp, the light from which is focused to form a circular spot on the skin. The light beam can, however, be interrupted by any one of nine narrow band spectrum filters before it strikes the skin surface. The reflected light falls on a photocell and the current which this generates is passed onto and measured by the galvanometer unit. The reflectance with each of the nine filters is measured relative to that of a white standard and hence the percentage reflectance for each filter is obtained. By plotting the percentage reflectance against the dominant wave-lengths of the various filters a reflectance curve can be drawn. This curve gives complete data regarding the colour of a surface. Such a reflectance curve or some abstraction from it, has already been used for describing differences in skin colour (*Weiner* [1952], *Lasker* [1954]).

Although selection is probably acting on the reflectance scale phenotype there is no necessary reason why the genes responsible for human skin colour should be additive on this scale. Another measure of colour may then not only be interesting in itself, but, if some transformation of the reflectance scale is needed, may provide a guide to the particular function required or give biological meaning to a function discovered empirically. The amount of pigment in the skin provides such a measure for if the scattering effects of skin are always the same, difference in pigment concentration are solely responsible for differences in colour.

Unlike the other methods of measuring skin colour reflectance spectrophotometry can itself provide a method of accurately relating colour with pigment concentration. The nature of the relationship was found by determining the reflectance values of known concentrations of extracted melanin. Unfortunately pigmented skin was not available and the melanin had to be extracted from human hair. However, although the particular relationship between reflectance values and concentration may differ between skin and hair melanin, the type of relationship is likely to be the same. The melanin was extracted from the hair either by heating for 15 minutes with N.KOH in a boiling water bath, or by refluxing for 15 hours with 3N.HCl and centrifuging. Known concentrations were made up in KOH, which facilitates dispersal of the particles. In order to reproduce as closely as possible the effect of increased pigmentation in human skin a small glass cell of 1 mm thickness was placed

on the arm of a comparatively unpigmented person and reflectance values were obtained with various concentrations of melanin in the cell.

On plotting various functions of the reflectance values against concentration it was found that there exists a linear relationship between the reciprocal of the reflectance value (1/R) at any one wave-length and the melanin concentration. This applies at a very wide range of concentration when using the 608 and 609 Ilford filters (wave-lengths 655 and 685 mμ respectively) but only at the lower concentrations when using the other filters (601 = 425 mμ, 602 = 465 mμ, 603 = 485 mμ, 604 = 515 mμ, 605 = 545 mμ, 606 = 474 mμ, 607 = 595 mμ). It is preferable then to use a waveband at the red end of the spectrum for determining melanin concentration rather than one in the blue or green even though the band isolated by the 608 and 609 Ilford filters is wider (90 mμ) than that isolated by the others (40 mμ).

The linear relationship between the reciprocal of the reflectance values and melanin concentrations established experimentally is also to a certain extent justified on theoretical grounds. In the past various functions have been put forward which relate the reflectance of light by a dyed fabric to dye concentration. Skin, being a diffusely reflecting medium behaves optically as a fabric. *Atherton* [1955] has shown that all these functions may be reduced approximately to simple reciprocal functions of reflectance. The reciprocal for the reflectance for a diffusely reflecting medium is therefore analogous to the optical density of a transparent coloured medium.

It was also found that the background has a constant effect at any one wave-length irrespective of melanin concentration. Such factors therefore as skin haemoglobin will not disturb the relationship as long as the blood supply to the skin is effectively the same in the individuals compared.

The optical effects of the skin have been determined by covering the cell with a fresh piece of unpigmented epidermis. The amount of scattering this produces does not appear to change appreciably with varying concentration. The presence of the melanin granules above the epidermis in the above experiments as compared with their presence in and below the epidermis in vivo conditions is therefore not likely to be a source of great error.

The actual amounts of melanin in the living individual cannot as yet be accurately determined because the contribution made to the reflectance value by the blood and other skin pigments, and by the intact skin itself, though probably constant, is not known. However, it

is possible to determine different degrees of melanin pigmentation in a family or population relative to one or more individuals. Thus for instance in our family studies of negro × white marriages the reciprocal of the reflectance value of the Liverpool born mother has been taken as the zero base line from which to calculate the relative melanin concentration of the West African father and the hybrid children.

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Discussion:

R. R. Gates (Cambridge, Mass.): I have made extensive observations of skin colour, have published reflectance curves of Negroes of mixed descent and Chinese, as well as a coloured chart of Negro-White skin colours (In *Pedigrees of Negro Families* 1949). There and in later papers I developed a tentative hypothesis involving 3 factors R, S, T having hypothethic melanin values of 6, 2, and 1, respectively. I also published with Dr. *A. A. Zimmermann* a histological study of skin specimens showing complete correspondence between depth of colour in the microscope and external phenotype. The interesting work of Drs. *Owen* and *Harrison* on the reflectance curves will no doubt give significant results, but I doubt if it will yield a *genetic* analysis.

D. F. Roberts (Oxford): 1. The most interesting work of *Harrison* and *Owen* represents marked progress towards the ending of the present unsatisfactory state of knowledge regarding the inheritance of skin colour, a state largely due hitherto to the absence of accurate objective measurements of this feature.

2. The actual reflectance values obtained for any individual are affected by a number of extraneous factors, such as the site of measurement. Were these taken into account when the data were collected?

3. The genetic interpretation to be given to the findings depends on the validity of the means and variances found for parental and hybrid groups. The extension of this work to larger numbers of individuals is therefore of the utmost importance.

G. A. Harrison (Liverpool): Although our measurements of skin colour with the E.E.L. spectrophotometer do not give a continuous reflectance curve over the whole spectrum, I am sure that Dr. *Roberts* will agree that since the concentration of melanin is proportional to 1 R at each of the 9 wave bands used, from the blue to the red, the same relationship, probably holds for the whole spectrum. Since however the relationship (at 400–500 mμ) is disturbed at very high concentrations and there is the possibility of another pigment being present in the hybrids with absorption in the blue; we have used the reflectance values at the red end of the spectrum for the genetic analysis and it is at a wavelength of 700 mμ that the genes for skin colour are additive on the R, I/R, and Log_{10} I/R scales and shown dominance to the white.

We are sure that our estimate of the negro variance is too high because we have included all West Africans and the figures that Dr. *Barnicot* has kindly allowed me to quote from his Yoruba sample represent a more reliable population variance. Nonetheless the Negro variance is significantly greater than the white variance. The very high first generation hybrid within family variance is presumably due to segregating modifiers from the white parent in whom, however, they have little or no expression, but I agree with Dr. *Barnicot* that if there is a large number of effective factors for skin colour the within family variance in our segregating families has probably been underestimated and this may account for the very similar within family variances of first generation and subsequent generation hybrids.

All the measurements used in the genetic analysis were taken on the medial aspect of the upper arm but analyses made at other sites would appear to be very similar.

Gates, R. R.: Acta genet. *6*, 485, 1956/57

Cambridge, Massachusetts, U.S.A.

RECORDS OF Y-INHERITED HAIRY EARS IN INDIA[1]

By R. R. GATES

In 1907, Tommasi published an account of an Italian family with 11 cases of hairy ears, all males, in five generations. This was one of the few cases of inheritance in the Y-chromosome and was found to be associated with alcoholism and insanity.

While traveling in Africa last year I happened across three unrelated cases of hypertrichosis of the ears in natives of India, two of whom were from Goa. In these three families the inheritance was compatible with Y-chromosome inheritance. Two further cases have since been reported to me. It therefore appears that hairy ears, with long black hairs in the rim of the ear, and showing holandric inheritance, is not uncommon in Goa and adjacent parts of India. There is no evidence of association with any abnormal mental condition.

In the Italian psychiatric literature of sixty years ago several other cases of hairy ears are cited, all of them associated with alcoholism, criminality, insanity or epilepsy. This association may have been fortuitous, resulting from the views of *Lombroso*. In any case holandric hairy ears were not very uncommon in Italy at that time. A modern survey is desirable to determine the frequency of this condition in Italy and also whether there is any significant association with mental aberration.

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Maltarello, A.: Acta genet. *6*, 486–491, 1956/57

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ASPECTS GÉNOTYPIQUES DU DÉVELOPPEMENT OSSEUX CHEZ LES JUMEAUX MZ ET DZ

Par A. MALTARELLO

Ayant à ma disposition le vaste matériel gémellaire de l'Institut «Mendel», j'ai voulu reprendre les observations faites par d'autres auteurs, par *Buschke* en particulier, au sujet des noyaux d'ossification.

La radiographie du poignet est suffisante pour suivre un développement osseux normal et subnormal.

«La main – comme l'écrit *Brandenberger* dans le grand traité du *Schinz* - est le *test* pour juger de la formation des noyaux d'ossification et de la maturation du squelette.»

Disposant, en effet, de sujets qu'on peut juger normaux, j'ai soumis chaque couple à la radiographie de la main droite, exécutée en même temps et sur le même cliché.

Mon matériel comprend 58 paires de jumeaux MZ dont 29 mâles et 29 femelles, 16 paires de jumeaux DZ unisexuels dont 12 mâles et 4 femelles et 24 paires de jumeaux DZ bisexuels toutes comprises entre 2 et 18 ans.

Suivant le système classique des recherches gémellaires, j'ai tout d'abord comparé, dans chaque paire, les deux éléments l'un vis-à-vis de l'autre, en relevant la concordance ou la discordance du développement osseux relatif.

Les résultats analytiques de ces observations sont exposés dans les tableaux annexes (tableaux 1, 2 et 3).

Les résultats d'ensemble sont représentés dans les deux diagrammes suivants:

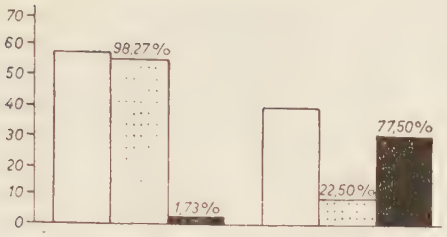

Fig. 1 *Fig. 2*

Diagramme 1: Des 58 paires MZ: 57 sont concordantes et une seulement ne l'est pas ce qui signifie un pourcentage de 98,27 % de concordance et de 1,73 % de discordance. – *Diagramme 2:* Les paires DZ, globalement considérées, présentent au contraire 22,50 % de concordance contre 77,50 % de discordance.

Soulignons la très haute concordance des jumeaux MZ qui se manifeste non seulement sous l'aspect quantitatif mais encore en ce qui concerne la forme et la structure des os. Il faut, par contre, souligner la discordance remarquable entre les jumeaux DZ qui, dans les paires de sexe différent, atteint 83,34 %.

Il est pourtant confirmé, en base aussi à nos données, que le processus de croissance osseuse se développe sous l'influence et le contrôle de facteurs génotypiques d'où la grande importance de l'âge osseux pour évaluer les troubles de croissance et pour établir les corrélations physiologiques avec le développement d'autres systèmes. En suivant quelques-unes des paires examinées, j'ai relevé comment la concordance et respectivement la discordance se maintiennent, avec de très faibles oscillations pourtant.

En conséquence de cette première série d'observations, il me semble pourtant devoir confirmer ce que *Buschke* avait déjà indiqué, c'est-à-dire que la comparaison radiographique des mains et éventuellement d'autres segments du squelette (pieds, crâne) peut utilement aider à la diagnose du zygotisme en complément évidemment d'autres données plus significatives.

Une deuxième série d'observations découle de la comparaison, à d'autres points de vue, de nos radiogrammes.

En voici schématiquement les résultats:

A. *Comparaison entre les paires MZ masculines et les paires MZ féminines de même âge:* Jusqu'à 7 ans, on relève une discordance complète due à une maturation précoce et constante des couples féminins. A partir de 8 ans, on constate, au contraire, une bonne concordance toujours avec une précocité relative des couples féminins.

Tableau 1. MZ.

Age	♂	Conc.	Disc.	♀	Conc.	Disc.	Total ♂+♀	Conc.	Disc.
2	1	1	–	–	–	–	1	1	–
3	1	1	–	1	1	–	2	2	–
4	4	4	–	–	–	–	4	4	–
5	2	2	–	3	3	–	5	5	–
6	3	2	1	4	4	–	7	6	1
7	4	4	–	–	–	–	4	4	–
8	4	4	–	4	4	–	8	8	–
9	2	2	–	4	4	–	6	6	–
10	1	1	–	4	4	–	5	5	–
11	3	3	–	3	3	–	6	6	–
12	2	2	–	2	2	–	4	4	–
15	–	–	–	2	2	–	2	2	–
16	2	2	–	–	–	–	2	2	–
18	–	–	–	2	2	–	2	2	–
Total	29	28	1	29	29	–	58	57	1
%		96,55 %	3,45 %		100 %	0,00 %		98,27 %	1,73 %

B. *Comparaison entre les paires MZ et les paires DZ unisexuelles et de même age:*

1. *toutes de même sexe:* discordance complète jusqu'à 8 ans autant pour les paires masculines que pour les paires féminines: concordance discrète à partir de 9 ans.

2. *de sexe respectivement opposé:* Les paires DZ féminines présentent une maturation précoce en comparaison des paires MZ masculines tandis que les paires féminines MZ présentent une précocité analogue sur les paires masculines DZ de même âge.

C. *Comparaison entre les paires DZ bisexuelles et les paires MZ respectivement masculines et féminines de même age:* Notre casuistique ne présente pas d'observations nombreuses. Toutefois, nous avons trouvé ce qu'on pouvait légitimement attendre, c'est-à-dire une concordance croisée qui intéresse d'une part le mâle de la paire DZ avec la paire MZ masculine controlatérale et d'autre part la femelle de la paire DZ avec la paire MZ féminine.

En conclusion, soulignons que les facteurs génotypiques contrôlant le développement osseux agissent d'une manière différente sur les deux sexes réalisant une maturation plus rapide chez les femelles, maturation

Tableau 2. DZ unisexuel.

Age	♂	Conc.	Disc.	♀	Conc.	Disc.	Total ♂ + ♀	Conc.	Disc.
2	1	–	1	–	–	–	1	–	1
3	2	–	2	–	–	–	2	–	2
6	1	1	–	1	–	1	2	1	1
7	3	1	2	1	1	–	4	2	2
8	2	–	2	1	1	–	3	1	2
9	–	–	–	1	1	–	1	1	–
10	1	–	1	–	–	–	1	–	1
11	1	–	1	–	–	–	1	–	1
14	1	–	1	–	–	–	1	–	1
Total	12	2	10	4	3	1	16	5	11
%		16,66 %	83,34 %		75 %	25 %		31,25 %	68,75 %

évidente surtout jusqu'à 8 ans environ et qui diminue ensuite progressivement sans disparaître complètement.

Il semble évident que la chose doit se mettre en rapport avec les caractéristiques hormonales particulières des deux sexes sur lesquelles s'exerce l'action des gènes. La preuve en serait faite surtout par la comparaison des paires DZ bisexuelles et des paires MZ respectivement masculines et féminines de même âge présentant la concordance croisée dont on a parlé ci-dessus.

Enfin, j'ai recherché s'il existait des différences et lesquelles entre l'âge osseux de nos sujets et celles de sujets mononés, de même âge chronologique.

Entre les différents systèmes, j'ai préféré, pour la rapidité de la consultation, le magnifique «Radiographic Atlas of Skeletal Development of the Hand and Wrist» de *Greulich* et *Pyle* qui peut très bien être appliqué aux sujets ainsi que l'a également constaté l'Ecole du Professeur *De Toni*.

Les résultats de ces comparaisons sont les suivantes:

- les paires MZ masculines sont en retard dans 38% des cas, les paires féminines ne le sont que dans 2% des cas seulement,
- la concordance avec le standard normal commence, pour les mâles à 7 ans environ et intéresse 54% des paires; pour les femelles, cette concordance commence à 5 ans environ et intéresse 86% des paires,
- les paires DZ masculines concordent avec le standard dans 50% des cas et les paires féminines dans 75% des cas,

Tableau 3. DZ bisexuel.

Age	paires	Conc.	Disc.
2	1	–	1
3	2	–	2
4	1	–	1
5	1	–	1
6	2	1	1
7	4	1	3
8	3	1	2
9	2	–	2
10	2	–	2
11	1	–	1
12	3	1	2
15	1	–	1
16	1	–	1
Total	24	4	20
%		16,66%	83,34%

– les paires DZ bisexuelles sont en retard dans 21% des cas et concordent dans 45% des cas,
– dans les autres 26% de ces mêmes paires, le mâle est en retard tandis que la femelle concorde.

Considérant d'une part l'ensemble des mâles et d'autre part l'ensemble des femelles appartenant aux paires observées, j'ai enfin trouvé:
– en avance: 1,8% des mâles contre 4,5% des femelles,
– en retard: 43% des mâles et 15% des femelles,
– en concordance avec le même âge osseux des radiogrammes standard: 58% des mâles et 72% des femelles.

Nos observations concordent largement avec celles des autres auteurs et confirment ce que j'ai dit plus haut.

Elles sont ultérieurement confirmées par les données relevées dans quatre groupes de triplets qui n'ont pas été comprises dans la casuistique précédente.

Le premier groupe, DZ unisexuel de 9 mois, comprend une paire masculine concordante et en même temps discordante avec le troisième mâle. Les membres de la paire MZ sont en harmonie avec le radiogramme standard de *Greulich* et *Pyle* tandis que le cojumeau DZ est en retard.

Le deuxième groupe est formé de triplets MZ de sexe masculin, observés à 5 et 6 ans, parfaitement concordants et tous en retard sur le standard.

Le troisième groupe, DZ bisexuel de 9 ans comprend une paire MZ féminine concordante et en même temps légèrement discordante avec le cojumeau DZ.

Dans le quatrième groupe, DZ bisexuel, contrôlé à 15 ans et 8 mois et à 16 ans et 10 mois, je n'ai pu étudier que la paire MZ masculine qui est trouvée concordante avec un léger retard sur le standard.

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Institute of Anatomy, University of Lund, Sweden

BODY-BUILD AND PHYSICAL ACTIVITY[1]

By B. LINDEGÅRD

In order to analyse the influence of habitual physical activity on body-build, 208 non-selected healthy 20-year-old Swedish men of different occupations were examined, soon after their arrival to military service and six months later, during which they had been subjected to ordinary military training. On the first examination the body-build was registered according to the method devised by *Lindegård* in 1953. On the second examination only the muscularity, i.e. the muscle factor, was re-examined.

According to the method cited, muscularity is determined by dynamometric recordings of the gross muscular strength of certain groups of muscles. In the present investigation, the "hand-grip", "shoulder-thrust" and "shoulder-pull" strengths were recorded.

It was supposed that there is a maximal and a minimal level of attainable muscularity for each individual, between which the actual muscularity varies in proportion to the degree of habitual physical activity. The results arrived at suggest that in the average individual, the actual muscularity of the "hand-grip" lies not far from the maximum level attainable, and the actual muscularity of the "shoulder-thrust" nearer the minimum level attainable, while the actual muscularity of the "shoulder-pull" has an intermediate position.

The correlation between skeletal sturdiness and muscularity seems to refer exclusively to the environmental-stable muscularity. That part of the interindividual variation of muscularity which is associated with a different habitual physical activity tends, instead, to camouflage the correlation between muscularity and skeletal sturdiness.

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[1] The paper will be published in Lunds Universitets Årsskrift N.F. 2, Vol. 52, 8, 1956.

Tanner, J. M.: Acta genet. *6*, 493, 1956/57

Institute of Child Health, University of London, Great Britain

PREDICTION OF ADULT BODY MEASUREMENT FROM MEASUREMENTS TAKEN EACH YEAR FROM BIRTH TO FIVE YEARS[1]

By J. M. TANNER

Forty-two men and thirty-eight women, previously measured at birth and every year up to five, have been remeasured as adults aged 25–30. The degree to which adult measurements of supine length, weight, forearm and foot lengths, head length and breadth, and shoulder and hip widths can be predicted from measurements in the first five years, has been examined by computing the following statistics:

(a) correlation coefficients between adult measurements and measurements at birth, 1, 2, 3, 4 and 5. Figures for supine length are respectively 0.27, 0.67, 0.77, 0.79, 0.81, 0.79.

(b) the percentage of the adult variance of a measurement accounted for cumulatively by regression on the measurement at birth, then birth and one year combined; 0, 1, 2 years, and so on. For supine length the figures are: at birth, 5%, by 1 year 45%, and subsequently 59%, 64%, 66%, 66%.

The conclusions are (i) size at birth is only very slightly related to adult size, or even size at 2, (ii) prediction of adult size is as good by age 3 as by age 5, (iii) *rate* of growth and adult size are independent.

Discussion:

F. Keiter (Hamburg): In Germany, a great deal of practical experience has been collected in predicting the future development of children by anthropologists in Paternity Testing. The conclusion has been drawn, that prediction may already be carried out with most certainty in children of 3 years, in this manner. The proof given by Mr. *Tanner* is of great importance.

[1] The paper has appeared in the Archives of Diseases in Childhood *31*, 372–381, 1956 in an extended form, with the title "Aberdeen Growth Study: I. The Prediction of Adult Body Measurements from measurements taken each year from Birth to Five Years", by *J. M. Tanner, M. J. R. Healy, R. D. Lockhart, J. MacKenzie* and *R. H. Whitehouse.*

Sontag, L. W. and *S. M. Garn:* Acta genet. *6*, 494–502, 1956/57

Fels Research Institute, Antioch College, Yellow Springs, Ohio, U.S.A.

HUMAN HEREDITY STUDIES OF THE FELS RESEARCH INSTITUTE

By LESTER W. SONTAG and S. M. GARN

There are various directions which research in human genetics can take. Discovering a new gene is always a pleasure, especially if a gene-enzyme relationship emerges. Comparing the frequencies of known genes, in different populations, makes human genetics an historical as well as a biological science, and leads to the study of ongoing evolution in man. And there are the basic problems of crossing-over, the mutation rate, the documentation of genetic drift, and the statistical demonstration that human mating may be influenced by chance but is never truly random!

Compared to these respectable pursuits, investigating the genetics of human behavior and the genetics of human growth represents research of a different order. Admittedly there are methodological problems, not ordinarily encountered, and a dependence upon research techniques borrowed from other disciplines. Time depth becomes important, as something to make use of, not avoid. We have been investigating the genetics of human behavior and the genetics of human growth for many years at the Fels Research Institute, with some measure of success and considerable satisfaction.

Basically the Fels Longitudinal studies revolve about 200 families, many of them related, and their progeny[1], now extending into the second generation. No claim is made for "random selection", rather, our subjects comprise a population about which a great deal is known. And because we have access to the subjects from before birth, right to the time they are parents in turn, time is on our side. We are not restricted to the study of traits which are unaffected by age, or limited to adults. Those very variables which plague other workers play into our hands. Siblings ordinarily are not of the same age, but given a few years we can obtain

age-constant data. Sex differences can be put in their proper place, through the use of normalized T-scores, so that the *rate* of long bone growth can be compared in siblings of unlike sex. And at present we are comparing the neonatal growth patterns of parents and offspring, having waited 20 years to complete these unique pairings.

Research into the genetics of human behaviour has in the past been unsatisfying, because of difficulties in measuring the characteristics investigated. As to normal behavior, about the most *measurable* dimension was "intelligence" as obtained from *Binet*'s tests or *Wechsler*'s. Our own studies at the *Fels*[2] show that the I.Q. is by no means a fixed aspect of the individual, and is capable of extraordinary changes during the growing period.

We have attributed many of these changes in intelligence to characteristics of personality structure as expressed in differently directed motivation, and have established causal relationships, but we believe that certain of the changes in measured intelligence are gene determined. Fig. 1 shows I.Q., height, appearance of ossification centers and the motor items of the Gesell tests on four siblings. In fig. 1a, the following facts should be noted. 1. The I.Q. rises tremendously (two S.D.) from three to five years. 2. The child is extremely tall and rapid growing (+ three S.D. in height). 3. It is very slow in motor development, especially at 18 and 24 months and it is extremely advanced in appearance of ossification centers. The same characteristics are shown in the other three sibs, fig. 1b, c, and d. We have then the familial pattern of rapid growth, excessive size, clumsiness and slow motor development. We believe that the early rise in I.Q., in these cases from three to five years, is in part, really the correction of an early depression in *Binet* performance due to the fact that the *Binet* test in the early years stresses motor activity and then shifts to more cognitive items. We are also convinced that the clumsiness and slow motor development cause an anxiety and lack of self-assurance which contribute to poor performance on the intelligence test. This factor tends to disappear as the child's motor control develops. Thus, we have what we believe to be a gene-determined (through the medium of excessive growth and slow development of motor skills) change in I.Q. performance. Many of the I.Q. changes after six years in our group of 200 children we have been able to relate to demonstrable personality patterns. However, we suspect that there may also be a gene determined maturational factor.

The autonomic nervous system, and its behavior during stress offer a very fruitful approach to the genetics of behavior. Heart rate, blood

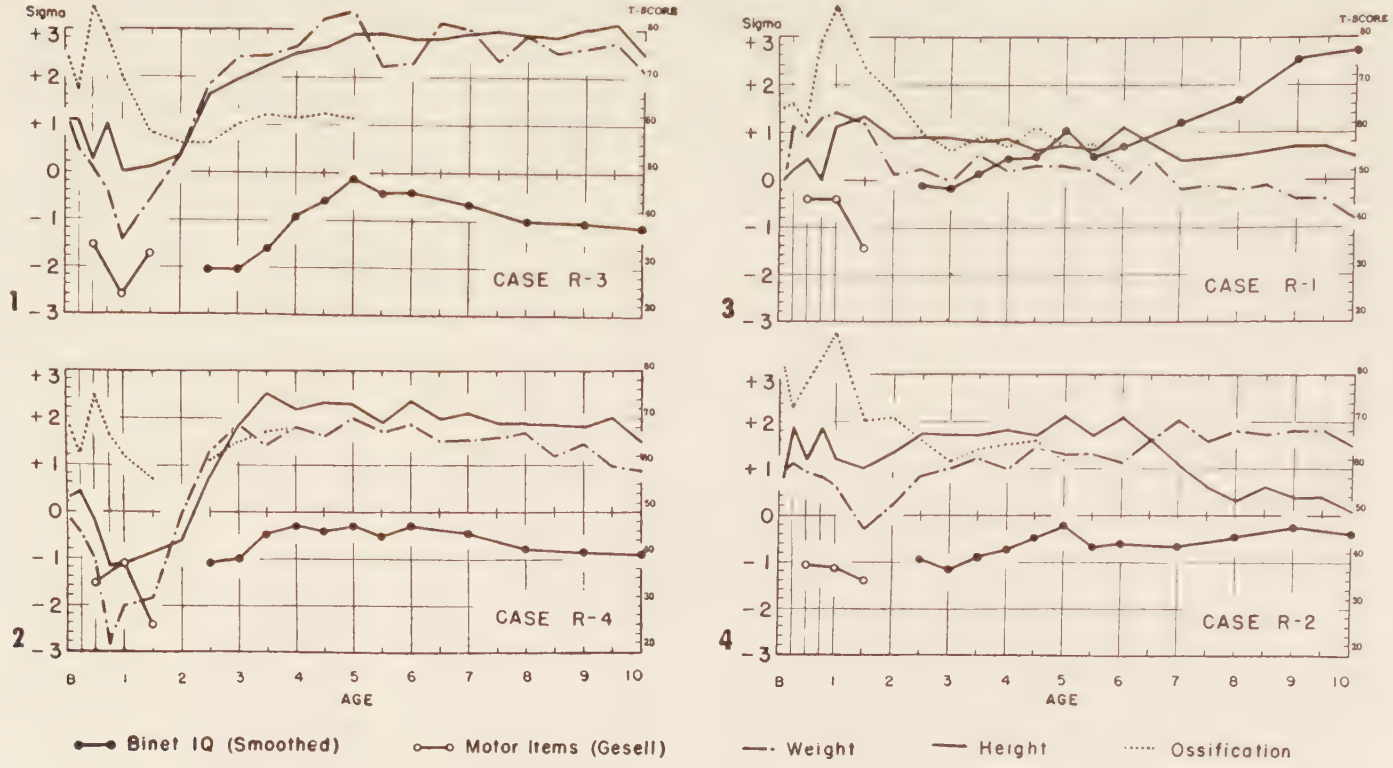

Fig. 1. Height, weight, ossification, *Binet* I.Q. and *Gesell* Motor Items in four siblings from birth to ten years.

pressure, the respiratory rate, cardiac output, gastric motility, sweat gland activity—these are measurable—and the changes during stress are measurable. Years ago we showed[3] that similarities in autonomic response increased with the degree of genetic relationship (fig. 2). Certainly such physiologic functions are important indications of how an individual *behaves*. Obviously, relevant data can be accumulated over a period of years, so that these sibling similarities, already in the literature, can be compared with parent-child similarities.

1940	Correlation	N
Twins	.434	5
Siblings	.255	10
Unrelated	.164	361
1941		
Twins	.470	5
Siblings	.406	19
Unrelated	.017	364
1942		
Twins	.489	6
Siblings	.288	25
Unrelated	.080	300

Fig. 2. Correlations of autonomic scores for twins, siblings and unrelated children in three different years. (Reprinted from Psychosomatic Medicine with permission of Paul B. Hoeber Inc., New York.)

Recently, *John I. Lacey*[4], at Fels, has shown that the *pattern of autonomic response* is characteristic of the individual, and fixed over a fairly long period of time. The five-year reproducibility of these patterns is as high as the immediate reproducibility! Here is an indication that many "psychosomatic" diseases stem not just from a particular kind of stress, or a particular parent-child relationship, but from an inherent and (presumably) gene-determined tendency to over-react in one branch of the autonomic nervous system. As we see it, the tendency for particular disorders such as ulcers, hypertension, and tachycardia to recur in families, is due to underlying patterns of autonomic response, which constitute only a potential danger until the individual is sufficiently stressed. From a practical point of view, discovering that X is a cardiac-reactor or a gastric-reactor might mean that we should take measures *in advance* to protect X's vascular or gastro-intestinal system.

As to growth, where information is easier to obtain, we have accumulated much evidence concerning its genic control. Again, the prob-

lem has been to deal with the meaningful aspects of growth, controlling age, as must be done. That siblings are similar in stature or weight and monozygotic twins more so is self-evident and of very little value just to demonstrate. Why are they similar or rather, where? Here the kind of work done by *Gruenberg* on the mouse, *Sawin* on the rabbit, and *Moulton*, *Shorland*, *Winchester* and others on more domestic animals is applicable to man. For we have long bones, vertebrae, muscle and fat, and through the medium of x-rays, individual bones, tissues and organs can be measured.

Some years ago we showed the extent of similarity in patterns of ossification[5] ,that is the sequence and time of appearance of the first 60 centers to appear (fig. 3). What center follows what is characteristic of the species, but within the species there is still a good deal of gene-determined individual variation.

Category	Number of Children	Mean Pearsonian Score
Monozygotic twins .	6	+.82
Total siblings . . .	24	+.32
Total nonsiblings . .	24	—.08

Using formula Mr = $\sqrt{\frac{\Sigma r^2}{N}}$ from Garrett, Henry E.: Statistics in Psychology and Education. New York 1937, Longmans, Green & Co., p. 284.

Fig. 3. The means of correlation coefficients of the Z scores of appearance times of 38 centers in twins, siblings and unrelated children. (Reprinted from Journal of Pediatrics, with permission of C.V. Mosby Company.)

Reviewing the literature, we are surprised to see how little has been done on the genetics of the size and *rate* of growth of the long bones in man. There is more, but little more on the vertebrae (especially the interpedicular widths) and this for adults. Breaking up the vertebral column into its segments (as we are doing) is exactly what *Sawin*[6] at the *Roscoe B. Jackson* Laboratory has done for rodents and his findings are surprisingly applicable to man.

Again bypassing our published studies on triplets and twins for lack of time and space, let us pass on to patterning. It is unfortunate that so little use has been made of triplet sets containing a monozygotic pair and an "odd" one, since such triplets include a built-in control. Repeatedly, we have encountered evidence that the "pattern" is gene-mediated[7] as distinct from time or amount. We have shown that the *pattern* of ossification was probably gene-determined, whereas the exact time of events

was much influenced by sex and maturity status. Similarly, the pattern or rather the *sequence* of tooth formation seems to be gene controlled[8], whereas the exact times are almost uncorrelated in siblings (fig. 4). P_2 forms before M_2 in some families and M_2 preceeds P_2 in others. Interestingly, families with the $M_2 > P_2$ sequence run high in missing second premolars. To our minds a missing tooth-"agenesis" is an extreme example of late formation, rather than an extension of the trait toward size reduction.

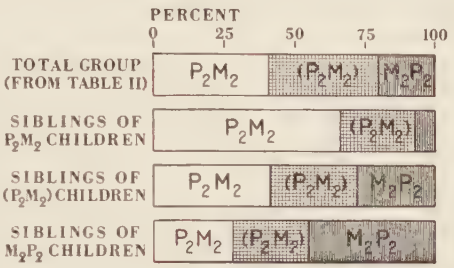

Fig. 4. Sibling similarities in the sequence of formation (calcification) of the mandibular molar and premolar teeth. Siblings are more likely to resemble each other in sequence of formation than chance would allow. (Reprinted from Journal of Dental Research with permission of C.V. Mosby Company.)

In fact, we have increasing evidence of the genetics of patterning from our studies of neonatal growth (fig. 5). Attempts to show sibling similarities in size or body composition have been rather unrewarding simply because infants vary greatly in maturational status at birth. Within a family of eight or nine siblings, there is a vast range of sizes during the first year due to variations in pregnancy and its duration, to recovery from birth trauma, and to subsequent growth. But compare fat to weight and a neat pattern emerges! Some families run to infants fat-for-their-weight, and some to the reverse[9]. Accidents of all kinds can determine how big a baby is at one, three or six months, but T-score fat to T-score weight shows unmistakable evidence of a common pattern. Other most extreme sibships run to (1) tiny, but fat infants and (2) long, but very lean infants. Both the longitudinal approach and the pattern concept are here illustrated.

But geneticists search for new marker genes. Apart from the blood groups, there are few traits of known mode of inheritance that are both non-pathologic and reasonably common. Quite by accident we discovered through sibling analyses, and the later incorporation of parental data that the tendency to form a foramen on the first cervical vertebra—as contrasted with the usual *sulcus*—is rather common and simply inherited. We believe that it is a Mendelian dominant with nearly complete penetrance (fig. 6). Our calculations suggest a gene frequency of 0.15 for this trait[10]. And since this foramen can be observed both in cadavers and

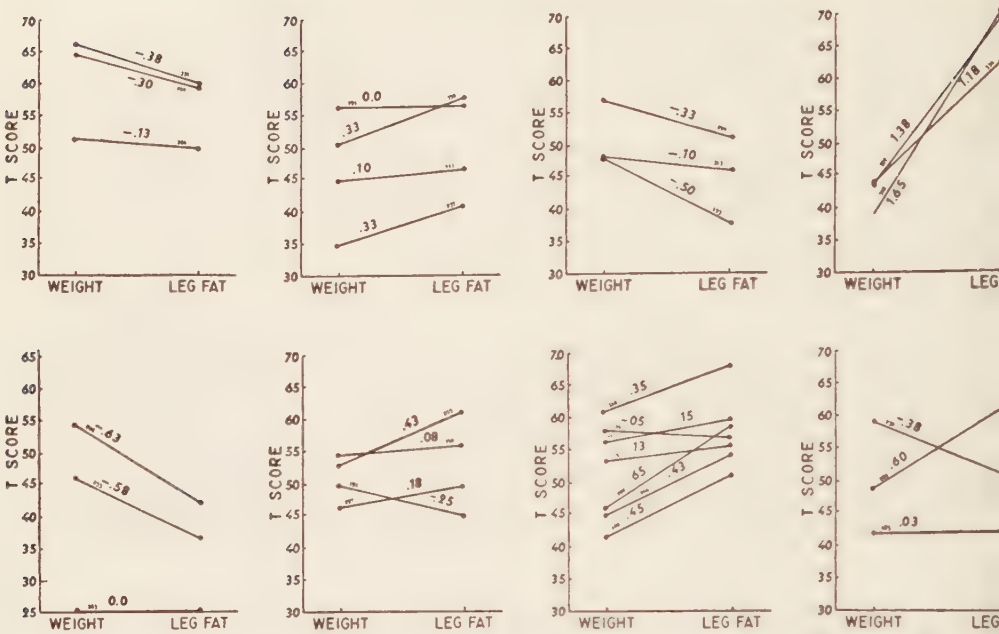

Fig. 5. T-scored profile patterns for fat and weight in infant siblings at nine months of age. Sibl are much more alike in fat-for-weight, than would be expected on a chance basis. And this holds e when they are markedly different in size as shown above. (Reprinted from the *Annals* of the New Y Academy of Sciences, with permission.)

skeletalized material and in the living alike (through the medium of x-rays) we believe that we have found a new and useful marker gene for man. Had we not accumulated sibling data, parental data, and had we no time depth in our study, this discovery surely would not have been made.

Conclusion

The genetics of human behavior, admittedly difficult to investigate, becomes somewhat easier when measurable behavioral variables are used, and when time is allowed to work for the investigator, giving him age-constant data, or at least sibling pairings of comparable age. Similarly, instead of waiting until growth has ceased, as is so often done, growth rather than size can be investigated—during the growing period—through the use of longitudinal data, coupled with a little patience. Insistence on traits not affected by age or sex, while important to the population geneticist, results in ignoring most of the human life span and the possibilities inherent therein.

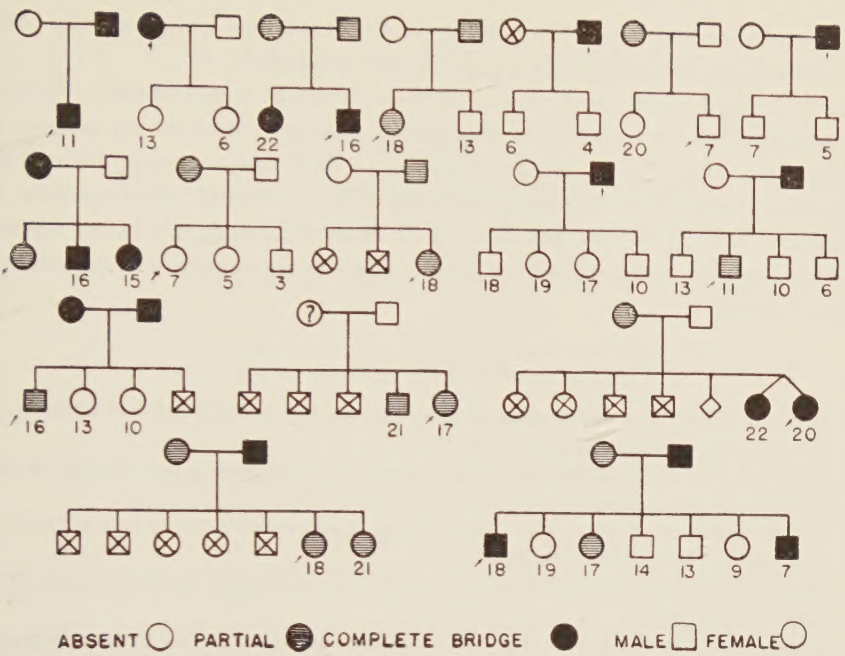

Fig. 6. Selected pedigrees showing the inheritance of the bridging trait of the first cervical vertebra: this trait is fairly commonplace (circa 26 %) and appears to be a simple autosomal dominant. (Reprinted from the American Journal of Physical Anthropology with permission of the Wistar Institute.)

A longitudinal study need not be set up as an investigation in human genetics. Especially, it should not be conceived simply as a vehicle for the further investigation of the known genes in man. A geneticist working under such conditions may be expected to develop such disorders as his autonomic response pattern would predict. But if longitudinal growth studies are properly conceived, and if due advantage is taken of siblings and parent-child comparisons much can be added to our knowledge of genes in man.

The Fels Longitudinal studies were not set up solely as a medium for genetic research. Psychologists, biochemists, physiological psychologists and physical anthropologists have reaped most of the investigative harvest as may be seen in more than 250 publications to date. Yet, repeatedly, we have been able to add new chapters to human genetics, ranging from the genetics of the autonomic nervous system to a new (and rather common) marker gene in man. What we have to offer is evidence

of how much can be gained from longitudinal studies, as apart from those instantaneous samplings more commonly employed.

In biological research, one is advised to select a genetically constant organism. Were we to follow this advice, there would be no science of human genetics! Again, we are advised to seek age-constant organisms, restricting ourselves to young sexually-mature adults. One purpose of this paper is to show how much can be lost by following this latter advice, and how much can be gained by the genetical investigation of longitudinal data on man.

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At the other end of the alimentary tract, it is difficult to realize that it is less than 20 years ago that we first began to control bacillary dysentery with sulphaguanidine, and from this beginning through the use of other sulphonamides and the new antibiotics, have come those great advances in surgical technique which now enable the surgeon to perform with a minimum risk, such major procedures upon the alimentary tract as total colectomy at one operation.

The surgical treatment of ulcerative colitis and the success of gluten-free diets in steatorrhoea represent other notable advances in treatment, just as the brilliant techniques of biliary and portal radiography take us further in our understanding of liver disease."

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